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September 11, 2000

Mr. John Leahy
SRRD/RB1
Document Processing Desk
Office of Pesticide Programs (7504C)
USEPA
Ariel Rios Building
1200 Pennsylvania Ave., N.W.
Washington, D.C. 20460

Re: Thiophanate-methyl (Chemical No. 102001)
Error comments on draft RED document received August 8, 2000

Dear Mr. Leahy:

Enclosed please find two copies of the results of Elf Atochem's review of the draft RED document for errors. Our response is divided into the following Sections:

Section A -
Error comments on the EFED Science Chapter for Thiophanate-Methyl dated May 22, 2000, DP Barcode 230325

Section B -
Error comments on the Anticipated Residues, Acute and Chronic Dietary Risk Assessments for Thiophanate-methyl (TM) and its Metabolites Methyl 2-benzimidazolyl carbamate (MBC) and 2-Aminobenzamidazole (2-AB) dated February 8, 2000, DP Barcode D262958
*Including attachments: Table 1, Table 2, Table 3, and current % CT data from National Center for Food and Agricultural Policy, *Business Confidential memo from Gustafson giving information on planting and treating acreage on potatoes.*

Section C -
Error comments on Thiophanate-Methyl - REVISED Report of the Hazard Identification Assessment Review Committee dated December 16, 1999

Section D -
Error comments on Drinking Water Assessment for Thiophanate-Methyl dated Sept. 21, 1999, DP Barcode D259653

Section E -
Error comments on THIOPHANATE-METHYL HED Product Chemistry and Residue Chemistry Chapters of the RED dated June 16, 2000, DP Barcode 230335

Section F -
Error comments on THIOPHANATE-METHYL CASE #2680 Revised Toxicology Chapter for the Reregistration Eligibility Decision Document dated December 21, 1999, DP Barcode D261951

Section G -
Error comments on Thiophanate-methyl: Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision Document dated June 21, 2000, DP Barcode D264018
*Including attachments: Current % CT data from National Center for Food and Agricultural Policy, *Business Confidential letter dated June 13, 2000 from Cleary Chemical giving definition of Residential Use Pattern, memo dated Sept. 5, 2000 from L. Castro of Elf Atochem accompanying a sample PHED run, copy of draft ARTF DFR protocol, and *Business Confidential memo from Gustafson giving information on planting and treating acreage on potatoes.*

Section H -
Error comments on Occupational and Residential Exposure Assessment and Recommendations for the Risk Assessment Document for Carbendazim (MBC) dated June 21, 2000, DP Barcode D265419

Section I -
Error comments on THIOPHANATE-METHYL - Report of the FQPA Safety Factor Committee dated July 1, 1999, HED Doc. No. 013546

Section J -
Error comments on Thiophanate-methyl: Preliminary Risk Assessment for the Reregistration eligibility Decision (RED) Document dated June 22, 2000, DP Barcode D230340
Including attachment: Current % CT data from National Center for Food and Agricultural Policy.

Section K -
Error comments on Revised Chronic Carcinogenic Dietary Risk Assessments for Thiophanate-methyl (TM) and its Metabolites Methyl 2-Benzimidazolyl Carbamate (MBC) and 2-Aminobenzamidazole (2-AB) dated May 10, 2000, DP Barcode D265906

There were no error comments on the incident reports section.

Elf Atochem did not identify any Confidential Business Information in the draft RED document. However, there are two attachments we are submitting which we must claim as CBI because it contains marketing information. They are indicated above by a (*) and is so marked in the hard

copy.

The following studies will be submitted to EPA:

Limited Field Rotational Crop - October, 2000
Consumer Practice (washing) Study in Apples - September, 2000
In Vitro Skin Penetration of Thiophanate-methyl - September, 2000
Thiophanate-methyl Mouse Micronucleus Test - September, 2000
Additional Grape Residue Studies

Please contact me if you need any clarification or additional information.

Very truly yours,

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cc: L. Castro, B. Sears, D. Olson, S. Ampofo,
M. Hattori, T. Tsujikawa

ERROR COMMENTS
SECTION A
EFED Science Chapter for Thiophanate-methyl, dated May 22, 2000, DP Barcode 230325.

No.	Location	Error
1	p. 3	The Chapter lists apples as representative of citrus. Please note that thiophanate-methyl is not registered on citrus and has no tolerances.
2	p. 3, ¶ 3	Line 7: The half-life of thiophanate-methyl, as determined in an apple dislodgeable foliar residue (DFR) dissipation study conducted in Washington, was less than 31.4 days. The decline curve was carefully evaluated and determined to be biphasic. The decline of thiophanate-methyl between the second application and 28 days after the second application was 17 days. This value is also comparable to the residue decline of 12 days calculated between the first and second application. The correlation coefficient associated with the residue decline after the second (last application) is very good r^2 (0.9372 for an r=0.9681) whereas the correlation coefficient for the decline curve when extended to include all data points up to the final sampling at 84 days is poor.

No.	Location	Error
3	p. 3, ¶ 3	Line 7: Elf Atochem performed two dislodgeable foliar residue studies on apples and two studies on strawberries. For modeling purposes, EPA has utilized the DFR study with the longest calculated half-life for a worst case assessment. Even so, certain scenarios assessed by EPA are inappropriate given the data set available to the Agency. For example, utilizing the DFR data from the Washington apple DFR study as surrogate data for North Carolina apple scenarios rather than a New York apple DFR study is inappropriate as the climatological conditions, which the Agency has portrayed as important, are far more similar between these two states. For the evaluation of wheat, beans, and onions, it would be more appropriate to consider the use of the strawberry DFR data as surrogate data rather than the apple DFR data. Wheat, bean, and onion foliage are much more exposed to sunlight than the apple leaves within a canopy. This would be even more likely for earlier applications to a growing crop, compared with a tree. The use of strawberry DFR data, which includes a study conducted in a drier California climate yielded much shorter half lives than that associated with the Washington apple trial. Within the strawberry DFR study submitted to EPA we noted that the DFR half-life is 0.94 days for a North Carolina site and residues were not detectable after 7 days. For the California site, the DFR half-life was 1.53 days and residues were at levels near the detection limit from 1 to 3 days post application. It is also important to note that at the North Carolina study site, MBC residues were at levels below the detection limits. Similarly, at the California site, MBC residues were less than the detection limit at 1 day. This information indicates that TM and MBC surface residues are very transient on crops exposed to sunlight; thus the EPA's ecological risk assessment using apples as surrogate data for wheat, beans and onions is greatly exaggerated. Also, in the case of the turf scenarios, it is inappropriate to use the DFR data associated with apples for turf. Instead, either the strawberry DFR data or studies turf transferable residue studies, that have been submitted to EPA , should be used to model the decline of residues on turf. The EPA has stated that strawberry DFR data reflects the residue decline associated with crops that have the potential for high levels of surface exposure to the sun. This would be true of turf. It should also be noted that a meaningful proportion of the food items such as tall grass, short grass, broadleaf plants are not target crops and would be associated with the crop rows. These food items would have significant exposure to the sun; therefore, residues would decline rapidly. This would even be the case for orchard crops where food items are found outside of the canopy. The fact that residues on food items would decline rapidly is well supported by turf transferable residue studies submitted to EPA. These studies not only demonstrate that turf residues decline very rapidly with half lives on the order of 0.3 to 7.9 days. The average half life value was only 2.2 days. Only very low levels of MBC were measured in any of these studies. This is a very important point which demonstrates that utilization of a high thiophanate-methyl/ MBC conversion factor as being utilized by EPA in the RED is inappropriate in this instance. The fact that MBC residues are lower probably relates to the fact that foliar photodegradation occurs through alternative degradatory routes that do not require MBC formation. Given the fact that thiophanate-methyl is not a benzimidazole, this is a distinct possibility.

No.	Location	Error
4	p. 4, ¶ 1	The statement that, "Estimated chronic hazards and risks to birds and mammals based on exposure to MBC are quite high" has not been demonstrated, since the risk assessments have not properly utilized the DFR data.
5	p. 4, ¶ 4	The statement that "TM is slightly to moderately toxic to aquatic organisms on an acute exposure basis." has not been demonstrated since the risk assessments have not properly utilized the DFR data.
6	p. 5, ¶ 1, line 6	The DFR half-life range for thiophanate-methyl is 0.94 days - 17 days. These values are associated with the first phase of a biphasic decline curve. We determined that a biphasic decline was the appropriate model for the data based on a statistical assessment of the correlation coefficients (r^2) values.
7	p. 5, ¶ 3	Tier II PRZM/EXAMS modeling was used to estimate surface water concentrations from use of TOPSIN M at maximum application rates and frequencies. The EPA assessment is based on a worst case assessment using a Koc of 117.7. Use of this Koc is highly conservative and represents a worst case evaluation. Thiophanate-methyl Kocs have been determined to range from 117.7 - 858.8 for a variety of soils. Elf Atochem intends to provide the EPA with a more refined modeling assessment which will include new use patterns that we wish to propose. Calculations of MBC residues in surface water based on the factor of 82.7% conversion of thiophanate-methyl to MBC are exaggerated as residues on soil that are exposed to sunlight yield a lower percent of MBC. This is evident based on review of the soil photolysis study, where at day 19.3, 23.6% of the total residue was thiophanate-methyl and only 20.8% of the residue was MBC. This was the highest level of MBC seen up to this final sampling point.

No.	Location	Error
8	p. 5, ¶ 4	The GENEEC model was used to estimate surface water concentrations from use of TOPSIN M use on turf and ornamental at maximum application rates and frequencies. GENEEC is a highly conservative model that considers the fate of chemical is a small, shallow, enclosed pond and does not consider typical dilution effects. The EPA assessment is also based on a worst case assessment using a Koc of 117.7. Use of this Koc is highly conservative and represents a worst case evaluation. Thiophanate methyl Kocs have been determined to range from 117.7 - 858.8 for a variety of soils. Elf Atochem intends to provide the EPA with a more refined modeling assessment which will include new use patterns that we wish to propose. Calculations of MBC residues in surface water based on the factor of 82.7% conversion of thiophanate-methyl to MBC are exaggerated as residues on soil that are exposed to sunlight yield a lower percent of MBC. This is evident based on review of the soil photolysis study, where at day 19.3, 23.6% of the total residue was thiophanate-methyl and only 20.8% of the residue was MBC. This was the highest level of MBC seen up to this final sampling point.
9	p. 6	The Chapter lists apples as representative of citrus. Please note that thiophanate-methyl is not registered on citrus and has no tolerances.
10	p. 7, ¶ 6, line 4	The listed numbers are MRIDs, not Accession Numbers.
11	p. 8, ¶ 3, line 5	Add reference to MRID 41482807, the main study.
12	p. 9, ¶ 2, line 4	Add reference to MRID 43545801, supplement.
13	p. 11, ¶ 3, line 4	No currently approved label includes these high rates for the southern states. The Agency has used a ‘dormant’, out of date label for this information. These rates should be removed from all calculations. In addition, the use of 12 applications is inappropriate since this is not a real-life scenario. Elf Atochem will provide more information.
14	p. 14, ¶ 2	There is no scientific justification for the use of grape agricultural practice data as surrogate data for onions. These are two very dissimilar crops with different agricultural considerations.
15	p. 15, line 3	Elf Atochem believes there may be a difference of interpretation on the “broadcast” onion rate and will address this in the near future.

No.	Location	Error
16	p. 17, line 9	No currently approved label includes these high rates for the southern states. The Agency has used a 'dormant', out of date label for this information. These rates should be removed from all calculations.
17	p. 18, table	For wheat: note that TM is not registered in ND on wheat.
18	p. 19, ¶ 2	Line 2: remove apostrophe from 'its'.
19	p. 21, ¶ 3, line 4	No currently approved label includes these high rates for the southern states. The Agency has used a 'dormant', out of date label for this information. These rates should be removed from all calculations.
20	p. 67	For Guideline 161-3, add MRID 41482807.
21	p. 74	Under COMMENTS section, 3rd comment: thiophanate-methyl is misspelled.
22	p. 80	Last paragraph: methanol is misspelled.
23	p. 83	Under COMMENTS: the 5th comment does not make sense.
24	p. 85	¶ 1, line 1: thiophanate-methyl is misspelled.
25	p. 85	Second chart: a 1993, Acceptable study on quail is not included, MRID 42930701.
26	p. 87	First chart: a 1993, Acceptable trout study is not included, MRID 42887001. After second chart: add appropriate parentheses. Under Freshwater Invert., Acute: an Acceptable study on TM should be included, MRID 42298101.
27	p. 89	MRID 42723701 is a study on MBC and the chart should so state.
28	p. 93	Table header is missing beginning parentheses. Item 1: this is a faulty assumption. It is equally valid to assume other species would be less sensitive. Appendix 8, item 3, line 2: 'potentially' is misspelled.
29	p. 94	Item 10: pesticides is misspelled. Item 11, line 2: "iof" is incorrect. Item 12, line 3: measured is misspelled. Item 13, line 2: variability is misspelled. Item 14, line 1: tern should be term.

ERROR COMMENTS
SECTION B
Anticipated Residues, Acute and Chronic Dietary Risk Assessments for Thiophanate-Methyl (TM) and its Metabolites Methyl 2-benzimidazolyl carbamate (MBC) and 2-aminobenzamidazole (2-AB), dated February 8, 2000, DP Barcode D262958.

No.	Location	Error
1	p. 2, line 3	Thiophanate-methyl is also registered for use on turf.
2	p. 2, line 5	Remove hyphen from Elf Atochem. Company name has actually changed to Elf Atochem North America Agrichemicals, a division of Atofina Chemicals, Inc. Elf Atochem is not the basic producer of TM; it is made by Nippon Soda Company, Ltd. of Japan.
3	p. 2; ¶ 2; line 7	MBC and 2-AB have the same toxicological end point as 2-AB and residues are assumed by EPA to be toxicologically equivalent.
4	p. 2; Executive Summary; Chronic and Cancer Dietary Exposure	Line 4 and 5: The old TM Q* was used to determine the cancer exposure value of 2.47 E-5. The value should be replaced with 1.6 E-6. This level is not statistically different from 1 E-6 and therefore is not at a level for concern for carcinogenic risk. It is the aggregate risk, as derived by EPA, that exceeds 2 E-6 and is at a level of concern for carcinogenic risk.
5	p. 2; Executive Summary; Chronic and Cancer Dietary Exposure	Line 4: The old MBC Q* was used to determine the cancer exposure value of 7.59 E-7. The value should be replaced with 4.7 E-7.
6	p. 3; Toxico-logical Informatio n¶ 1; line 8 and 9	The old TM Q* of 2.08 E-1 and old MBC Q* of 4.2 E-3 are listed. The new TM Q* of 1.38 E-2 and new MBC Q* of 2.39 E-3 should be listed instead. Elf Atochem is preparing comments concerning the calculation of the TM Q*

No.	Location	Error
7	**p. 4; bottom of Table 1**	**The old TM Q* of 2.08 E-1 should be replaced with the new TM Q* of 1.38 E-2**
8	**p. 4**	**Last line: add close parentheses.**
9	**p. 5, chart**	**ENDPOINT column, chronic dietary: did not finish sentence "...in both sexes of..."**
10	**p. 5; bottom of table 2**	**The old MBC Q* of 4.2 E-3 should be replaced with the new MBC Q* of 2.39 E-3.**
11	**p. 6**	**Line 1: the tolerances for cucumbers, melons, and squash are 1.0 ppm, not 0.1 ppm.** **Line 2: please note that all postharvest uses of thiophanate-methyl have been cancelled since 1992.** **Line 3: additional tolerances exist for bananas (2 ppm), green and dry onions (3 ppm), potato seed piece (0.05 ppm), pecans (0.2 ppm), sugar beets (0.2 ppm), wheat grain (0.05 ppm)and pumpkins (1.0 ppm).**
12	**p. 6; Residues of Concern; ¶1; line 5**	**EPA should be consistent with its procedure for determining 2-AB residues, either the TM or MBC ratio can be used, however, not both. MBC is closer along the metabolic route, and structurally to 2-AB than TM to 2-AB. For this reason, using the residue level of only MBC to calculate 2-AB residues would seem the most logical approach. Also, unlike TM, both compounds are benzimidazoles.** **Elf Atochem also believes that it is incorrect to include residues levels of 2-AB that were extracted through acidic reflux conditions. The bound residues are not soluble and would not be bioavailable when ingested.**

No.	Location	Error
13	**p. 7; ¶ 2; line 3; Table 4**	**The use of surrogate crops is more appropriate for calculating 2-AB residue levels. For example, using sugar beets for determining 2-AB residues in peaches is inappropriate when apple data is available. Elf Atochem metabolism studies cover general crop groupings. Apples for fruits and nuts; beans as a row crop; sugar beets as a root crop; and wheat as a grain. The appropriate metabolism studies should be used for the assessment of 2-AB residues for all crops. Table 4 should be appropriately revised. This approach would be consistent with EPA policy concerning the use of metabolism studies to represent the nature of the residue in general crop groupings. EPA used this approach properly for processed plums by using the apple metabolism study for 2-AB calculations , but then improperly for stone fruit RAC data used the sugar beet metabolism study for calculating 2-AB residue levels.**
14	**p. 8; Sources of Residue Data; ¶1; line 1**	**Monitoring data from USDA Pesticide Data Program (PDP) is available for MBC residues for certain food commodities. This data should be used for developing a more accurate risk assessment of MBC residue dietary exposure. It is also possible to approximateTM residues at the consumer level by using the average ratio of TM to MBC within residue studies and applying the ratio factor to the PDP data. Because thiophanate-methyl residues dissipate more rapidly than MBC residues, such an assessment would still be very conservative.**
15	**p. 8, ¶ 3**	**Line 3: Add an 's' to the end of 'trial'.**
16	**p. 8, ¶ 4**	**Line 2: Elf Atochem has not cancelled the use on bananas.**
17	**p.8, Table 5**	**Field trial work has been conducted for Green Onions (discussed further in "Bulb Vegetable" section, summary attached as Table 1) and will be submitted.**
18	**p.8, Table 5**	**field trial data are available for Soybeans (MRID #44572701) (discussed further in "Legume Vegetable" section, summary attached as Table 2)**
19	**p. 10**	**Last line of Percent Crop Treated Data paragraph: add a 't' to the end of 'assessmen'.**

No.	Location	Error
20	**p. 9, line 2**	**processing studies have been conducted for peanuts (MRID #44850901), potatoes (MRID # 44498502), soybeans (MRID #44572702), and sugar beets (MRID #44584601). In addition, a washing study has been conducted for apples (to be submitted).**
21	**p.10, lines 9 and 10 after the table**	**Processing factor=prunes/plums MBC+2AB should be 1.73 (not 1.72)** **Processing factor=prunes/plums TM should be 0.014 if the residues in the two studies are averaged, and the processing factor is based on the average residues. The equation on p. 10 solves to 0.28, not the incorrect value of 0.17 listed in the review.**
22	**p. 10 after prunes discussion**	**The following summary calculations should be added, based on the additional submitted processing studies:** **<u>potatoes</u> (residues not detected in trial conducted at 10X the maximum use rate--cannot calculate processing factors, but it is reasonable to at least assume no concentration in dried potato products and change the default to 1.0.)** **<u>soybeans</u>: *Reserved beans*: 2-AB=0.92 x 1.6 ppm=1.47; MBC+2-AB=1.6ppm+1.47ppm=3.07ppm. *Meal*: 2-AB=0.92 x 1.0 ppm=0.92 ppm; MBC+2-AB=1.0 ppm+0.92ppm=1.92ppm. *Refined Oil*: 2-AB=0.92 x 0.025=0.06 ppm; MBC+2-AB = 0.025 ppm + 0.06 ppm = 0.09ppm.** **Proc. Factor=meal/bean=1.92/3.07=0.63 for MBC+2-AB** **Proc. Factor=meal/bean=1.3/3.8=0.42 for TM** **Proc. Factor=refined oil/bean=0.09/3.07=0.03 for MBC+2-AB** **Proc. Factor=refined oil/bean=0.07/3.8=0.02 TM** **<u>sugar beets</u>: averaged two studies, however, the 1992 study is most representative because beets were processed shortly after harvest** ***RAC*:** ***Sugar*:** **Proc. Factor=sugar/beet=0.06/0.43=0.14 (92); 0.06/0.42=0.15 for MBC+2-AB(97); average factor=0.14** **Proc. Factor=sugar/beet=0.025/1.065=0.02; 0.025/0.685=0.04; average factor for TM = 0.03** **(see Table 3)** **Note: these calculations do not take into account our proposal for how 2-AB residues should be calculated. We believe EPA's calculations should be revised further in this respect.**

No.	Location	Error
23	**p.10, Percent Crop Trtd**	**The most current data should be used in the risk assessment. Table 18B: "Pesticide Use in Crop Production By Active Ingredient and Crop, 1997 Summary, Thiophanate Methyl" published by NCFAP (L. Gianessi) (Attached to this document as Table 4)** **This would result in the following revised values: cherries (1% CT), apricots (3% CT), nectarines (1% CT), peaches (5% CT).** **Data are available to replace the default 100% CT for the following crops:** **sugarbeets (9% CT)** **cucumbers (1% CT)** **squash (1% CT)** **Use of TM on onions is so small that there are no reports for usage even though major producing states are surveyed. We recommend setting the default at 1% CT.**
24	**p. 11, line 3**	**The word 'experienced' should be replaced by 'expressed'.**
25	**p.11, Root and Tuber Vegetable Group - Potatoes**	**EPA apparently only reviewed one potato study (MRID 44468202). A second study was conducted with combined seed piece treatment and foliar applications (MRID 45061901). Residues were not detected in any treated samples.** **<u>Acute dietary exposure</u>-** ***TM*-An RDF should be created with 25 repeated ½ LOQ residue levels at 0.025 ppm and 225 zeros to reflect 10% CT for potatoes.** ***MBC+2-AB*-An RDF should be created with 25 repeated residue levels of 0.044 ppm and 225 zeros to reflect 10% CT for potatoes.** **<u>Chronic dietary exposure</u>-** ***TM*-use the average value of 0.025 (1/2 LOQ) adjusted by 10% CT (0.025 x 0.10)=0.0025 ppm.** ***MBC+2-AB*-Use the average value of 0.044 adjusted by 10% CT (0.044 x 0.10)=0.0044 ppm** **Note: these calculations do not take into account our proposal for how 2-AB residues should be calculated. We believe EPA's calculations should be revised further in this respect.**
26	**p.12, Sugar Beets**	**Sugar beet field trials (MRID 44643501) have been submitted to EPA. A processing study is also available (MRID 44584601). Using a conversion factor 2-AB/MBC=1.45, the mean residue in sugar beet roots is 0.063 MBC+2-AB. TM levels are 0.028 ppm. These values should be used in both the acute and chronic exposure assessments. Adjust by 9% CT. (See Table 3)**

No.	Location	Error
27	**p. 13, table**	**Lima bean metabolism data should be utilized for calculating 2-AB residues in onions. Only the MBC/ 2 AB ratio should be used.**
28	**p. 13, line 5**	**Green onion data are available (will be submitted) and do not need to be translated from dry bulb onion data. See Table 1 for calculations of MBC+2-AB. Acute analysis: RDF file should be set up for TM with 1 ½ LOQ residue (0.025 ppm) 5 residue values from the trials, and 54 zero values to represent 10% CT. RDF file for MBC+2-AB should have 6 detected residue values and 54 zero values. Chronic analysis: the mean TM value of 0.521 ppm adjusted by 10% CT (0.052 ppm) and the mean MBC+2-AB value 0.732 ppm adjusted by 10% CT (0.073 ppm). (See Table 1) Note: these calculations do not take into account our proposal for how 2-AB residues should be calculated. We believe EPA's calculations should be revised further in this respect.**
29	**p. 13**	**Acute dietary exposure, section headed *MBC + 2AB*: there were not 8 detected residues, rather there were 2 detectable residues. 8 values were used based on the theoretical calculation for 2-AB residues.**
30	**p. 13, last sentence**	**Field trial data are available for soybeans (MRID 44572701). Dry bean field trial data have been accepted by EPA to represent PHI=28 days (see EPA memo 6/17/97) Table 6 summarizes the study trials. Acute and chronic analysis: should be a point estimate for blended commodity, 0.025 ppm TM and 0.065 ppm MBC+2-AB adjusted to reflect 9% CT Note: these calculations do not take into account our proposal for how 2-AB residues should be calculated. We believe EPA's calculations should be revised further in this respect.**
31	**p. 14, table**	**Only MBC/ 2 AB ratio should be used from metabolism study.**
32	**p. 14 lima beans**	**In the table at the top of the page, bottom line of the table: the trial with 0.07 MBC and <0.05 TM represents 21 days rather than the 14 days and should not be included in RDFs or calculations of anticipated residues. Removal reduces the mean TM to 0.025 ppm.**

No.	Location	Error
33	**p.15, soybeans**	**Field trial data are available for soybeans (MRID 44572701). See Table 2 for calculations of MBC+2-AB. Acute and chronic analysis: should be a point estimate for blended commodity, 0.03 ppm TM and 0.083 ppm MBC+2-AB adjusted to reflect just 1% CT (0.0003 ppm and 0.0008 ppm, respectively). Note: these calculations do not take into account our proposal for how 2-AB residues should be calculated. We believe EPA's calculations should be revised further in this respect.**
34	**p. 16; table**	**Only MBC/ 2 AB ratio should be used from metabolism study.**
35	**p. 17; table**	**Lima bean metabolism data should be utilized for calculating 2-AB residues in cucumbers. Only the MBC/ 2 AB ratio should be used. It is not clear where the factors of 0.74 and 0.43 used in chronic risk assessment came from.**
36	**p. 17, cucumbers**	**Acute dietary exposure- should be 990 zeroes in the RDFs for TM and MBC+2-AB because NCFAP data show 1% CT for cucumbers. Chronic dietary exposure - the average MBC+2-AB should be 0.066 ppm (not 0.052 ppm) adjusted by 1% CT to 0.0007 ppm. Note: these calculations do not take into account our proposal for how 2-AB residues should be calculated. We believe EPA's calculations should be revised further in this respect.**
37	**p. 18; table**	**Lima bean metabolism data should be utilized for calculating 2-AB residues in watermelon. Only the MBC/ 2 AB ratio should be used. It is not clear where the factors of 0.74 and 0.43 used in chronic risk assessment came from.**
38	**p. 19; table**	**Lima bean metabolism data should be utilized for calculating 2-AB residues in summer squash. Only the MBC/ 2 AB ratio should be used. It is not clear where the factors of 0.74 and 0.43 used in chronic risk assessment came from.**
39	**p. 19, table for squash**	**In line 5 under MBC, the value should be 0.23 (not 0.13). The MBC+2-AB value in the acute RDF should be corrected to 0.56 ppm. The chronic estimate for MBC+2-AB should be corrected to 0.40 and the corrected mean value for squash is 0.095 ppm. Note: these calculations do not take into account our proposal for how 2-AB residues should be calculated. We believe EPA's calculations should be revised further in this respect.**

No.	Location	Error
40	**p. 20; table**	**Only the MBC/ 2 AB ratio should be used from metabolism study.**
41	**p.21; table**	**Apple metabolism data should be utilized for calculating 2-AB residues in cherries. It is not clear where the factor of 0.74 used in chronic risk assessment came from.**
42	**p. 21, table**	**The first line in the "cherries" table should be removed because it does not represent PHI=1 day. Under acute dietary exposure the LOQ value should be removed from both the TM and MBC+2-AB columns and the RDF adjusted to have 133 zeros. Chronic dietary exposure - the average value and % CT should be changed to 3.36 ppm x 1% CT for an average of 0.034 TM. The revised MBC+2-AB should be 1.1 ppm x 1 % CT= 0.011 ppm.** **Note: these calculations do not take into account our proposal for how 2-AB residues should be calculated. We believe EPA's calculations should be revised further in this respect.**
43	**p. 21, ¶ 2, last line**	**Remove the 'd' from the end of 'refined'.**
44	**p.22, nectarines**	**The first line in the "nectarines" table should be removed because it represents PHI=0 rather than PHI=1 day. In line 4 of the table, MBC value should be 0.09 ppm instead of <0.05 ppm. The corresponding MBC+2-AB calculations should be corrected, with the acute value being 0.22 ppm, and the chronic value at 0.16 ppm. One trial was not included in the table and thus should be added. The TM value is 1.44 ppm and the MBC value is 0.11 ppm. The corresponding calculations of acute and chronic MBC+2-AB should be corrected accordingly (acute MBC+2-AB should be 0.27 ppm, and chronic should be 0.19 ppm).** **For acute dietary exposure , MBC+2-AB, the RDF should have 4 detected residues, 4 residues at the ½ LOQ, and 72 zeros. For chronic dietary exposure, the revised average value of 0.081should be muliplied by 1% CT (from NCFAP studies) for 0.008 ppm for TM. The revised MBC+2-AB average value of 0.13 should be multiplied by 1 % CT to get a value of 0.0013 ppm (on p. 23).** **Note: these calculations do not take into account our proposal for how 2-AB residues should be calculated. We believe EPA's calculations should be revised further in this respect.**

No.	Location	Error
45	**p. 22; table**	**Apple metabolism data should be utilized for calculating 2-AB residues in nectarines. Only the MBC/ 2 AB ratio should be used. It is not clear where the factors of 0.74 and 0.43 used in chronic risk assessment came from. Footnote in table suggests that Apple metabolism data was used, but it was not.**
46	**p. 23; table**	**Apple metabolism data should be utilized for calculating 2-AB residues in peaches. Only the MBC/ 2 AB ratio should be used. It is not clear where the factors of 0.74 and 0.43 used in chronic risk assessment came from. Footnote in table suggests that apple metabolism data was used, but it was not.**
47	**p.23, peaches**	**In peaches table, first line, the acute 2-AB/TM conversion factor should be 0.83 (not 1.45) and the corresponding MBC+2-AB should be 0.11 ppm. In chronic dietary exposure - the NCFAP data show only 5% of peaches are treated. The estimate for TM should be recalculated as 0.0385 (0.77 x 0.05) and for MBC+2-AB the correct value is 0.018 ppm (0.359 x 0.05).** **Note: these calculations do not take into account our proposal for how 2-AB residues should be calculated. We believe EPA's calculations should be revised further in this respect.**
48	**p. 24, plums**	**For plums, chronic dietary exposure - the average value for TM should be 0.073 ppm (not 0.072 ppm) and should be adjusted by 1% CT (NCFAP report) for a residue value of 0.0007 ppm. The MBC+2-AB value should be 0.069 ppm adjusted by 1% CT for a residue of 0.0007 ppm.** **Note: these calculations do not take into account our proposal for how 2-AB residues should be calculated. We believe EPA's calculations should be revised further in this respect.**
49	**p. 24; table**	**Apple metabolism data should be utilized for calculating 2-AB residues in plums. Only the MBC/ 2 AB ratio should be used. It is not clear where the factors of 0.74 and 0.43 used in chronic risk assessment came from. Footnote in table suggests that Apple metabolism data was used, but it was not.**
50	**p. 25**	**Under Apricots, line 1: change '...use pattern as the same...' to 'is the same'.**

No.	Location	Error
51	**p. 25; Tree nuts Group; Almonds**	**Apple metabolism data should be utilized for calculating MBC and 2-AB residues in almonds.**
52	**p.25 apricots**	**The same corrected values for plums should apply to apricots since the data were translated--except that the NCFAP shows 3% CT for apricots. For chronic dietary exposure, the TM residue of 0.073 ppm should be adjusted by 3% CT (NCFAP report) for a residue value of 0.002 ppm. The MBC+2-AB value should be 0.069 ppm adjusted by 3% CT for a residue of 0.002 ppm.** **Note: these calculations do not take into account our proposal for how 2-AB residues should be calculated. We believe EPA's calculations should be revised further in this respect.**
53	**p.25, almonds**	**Almond data representing the current use pattern have been submitted to EPA (MRID 44487001). This section should be corrected to represent nondetected residues of TM or MBC in 10 trials with 9% CT from NCFAP for average crop treated. Application of the 2-AB/MBC=0.9 conversion factor to MBC results in MBC+2-AB=0.05 ppm (0.025 x 0.9). For acute dietary exposure, therefore, the TM RDF file should consist of 16 repeated LOQ values of 0.025 and 84 zero residues (to represent the EPA listed maximum 16.4 %CT) . The MBC+2-AB RDF file should consist of 16 repeated values of 0.05 ppm and 84 zero residues. For the chronic dietary exposure - for TM a value of 0.002 should be used (0.025 x .09 (9%CT)), and for MBC+2-AB a value of 0.0045 ppm should be used (0.05 x 0.09).** **Note: these calculations do not take into account our proposal for how 2-AB residues should be calculated. We believe EPA's calculations should be revised further in this respect.**

No.	Location	Error
54	**p.26, pecans**	**Field trial data are available at the current label rate (MRID 44498501).** **This section should be corrected to represent nondetected residues of TM or MBC in 10 trials with 4% CT from NCFAP for average crop treated. Application of the 2-AB/MBC=0.9 conversion factor to MBC results in MBC+2-AB=0.05 ppm (0.025 x 0.9). For <u>acute dietary exposure</u>, therefore, the TM RDF file should consist of 16 repeated LOQ values of 0.025 and 84 zero residues (to represent the EPA listed maximum 15.5 %CT). The MBC+2-AB RDF file should consist of 16 repeated values of 0.05 ppm and 84 zero residues. For the <u>chronic dietary exposure</u> - for TM a value of 0.001 should be used (0.025 x .04 (4%CT)), and for MBC+2-AB a value of 0.002 ppm should be used (0.05 x 0.04).** **Note: these calculations do not take into account our proposal for how 2-AB residues should be calculated. We believe EPA's calculations should be revised further in this respect.**
55	**p. 26; Tree nuts Group; Pecans**	**Apple metabolism data should be utilized for calculating MBC and 2-AB residues in pecans.**
56	**p. 27; Strawber-ries; table**	**Apple metabolism data should be utilized for calculating 2-AB residues in strawberries. Only the MBC/ 2 AB ratio should be used. It is not clear where the factor of 0.74 used in chronic risk assessment came from.**
57	**p.27, wheat**	**For <u>acute dietary exposure</u> - a point estimate of 0.00025 ppm should be used (0.025 ppm x 0.01 (%CT)) for TM (not 0.0004).**
58	**p.27, straw-berries**	**Line 5: In the strawberry table, bottom of page, the TM value should be 0.44 (not 0.45) ppm.**
59	**p.28; peanuts; table**	**Lima bean metabolism data should be utilized for calculating MBC and 2-AB residues in peanuts.**

No.	Location	Error
60	p.28, peanuts	Field trial data for peanuts at the maximum application rate, and PHIs close to the minimum are available (MRID 44515701). This section should be corrected to represent nondetected residues of TM or MBC in 10 trials with 1% CT (from NCFAP). Application of the 2-AB/MBC=0.9 conversion factor to MBC results in MBC+2-AB=0.05 ppm (0.025 x 0.9). For acute dietary exposure, therefore, the TM RDF file should consist of 5 LOQ value of 0.025 and 95 zero residues (to represent the EPA listed maximum 4.8 % CT). The MBC+2-AB RDF file should consist of 5 repeated values of 0.05 ppm and 95 zero residues. For the chronic dietary exposure - for TM a value of 0.00025 should be used (0.025 x .01 (1% CT), and for MBC+2-AB a value of 0.0005 ppm should be used (0.05 x 0.1).
61	p. 30, Table 7	The combined residues of MBC in whole milk was 0.034 ppm TM equivalents and for skim milk 0.044 ppm. Tolerance should be established as 0.1 ppm, not 0.15 ppm.
62	p. 30; Table 7	The combined residues of TM and MBC in muscle, fat, and liver was <0.045 ppm TM equivalents and <0.075 ppm in kidneys. Tolerance should be established at 0.1 ppm, not 0.15 ppm.
63	p. 31; Chronic and Cancer Dietary Exposure; ¶1; line 4	The old TM Q* was used to determine the cancer exposure value of 2.47 E-5. The value should be replaced with 1.6 E-6. This level is not statistically different from 1 E-6 and therefore is not at a level for concern for carcinogenic risk. It is the aggregate risk, as derived by EPA, that exceeds 2 E-6 and is at a level of concern for carcinogenic risk.
64	p.31; Chronic and Cancer Dietary Exposure	Line 4: The old MBC Q* was used to determine the cancer exposure value of 7.59 E-7. The value should be replaced with 4.7 E-7.
65	p. 33; Table 10	The old TM Q* was used to determine the cancer exposure value of 2.47 E-5. The value should be replaced with 1.6 E-6. The old MBC Q* was used to determine the cancer exposure value of 7.59 E-7. The value should be replaced with 4.7 E-7.
66	p. 31-34 Results/ Discussion	These results will change when corrections/additions are made to anticipated residues as noted in this memo.

No.	Location	Error
67	p. 35 RDF for lima beans	% CT is in error for TM, and a trial not at PHI=14 was accidentally included, the following are corrections that should be made when it is excluded: TM: TOTALZ=45; TOTALLOD= 4. MBC+2-AB: TOTALZ=45; remove 0.134 from residue list.
68	p.35, RDF for cherries	A trial not at PHI=1 was accidentally included, the following are corrections that should be made when it is excluded: TM: %CT=5; TOTALNZ=7; remove 0.025 from list of residues MBC+2-AB: TOTALNZ=7; remove 0.061 from residue list.
69	p.35, RDF cucumbers	The % CT for both TM and MBC+2-AB should be 1% CT; TOTALZ=990
70	p.36, RDF nectarines	A trial not at PHI=1 was accidentally included, another trial that should have been included was not. The following changes to the RDF files are needed: TM: remove the first value (1.33) and add a new value of 1.44. MBC+2-AB: remove the first value (0.49) and add a new value of 0.27 ppm. Also, the 4th value listed should be 0.22 instead of 1.10 ppm.
71	p.36, RDF onions	Change the % CT to 10%; for both TM and MBC+2+AB, the TOTALZ=72.
72	p. 36, RDF peaches	TM: TOTALNZ=10; the value 2.03 should be added to the bottom of the file. MBC+2-AB: the first residue value should be 0.11 (not 0.17)
73	p. 36 RDF squash	Apply the NCFAP 1 % CT for squash and change to TOTALZ=990 for both. For MBC+2-AB, correct 4th value down to be 0.56 ppm (not 0.319).
74	p. 37 RDF straw-berries	The 5th residue value listed for TM should be 0.44 ppm (not 0.45 ppm)
75	potatoes	An RDF was not included for potatoes--this should be set up with 11 values at the LOQ (0.025) for TM and 0.061 ppm for MBC+2-AB; and TOTALZ=99. The % CT should be 10%.
76	p. 53, Att #17	The old TM Q* was used to determine the cancer exposure value of 2.47 E-5. The value should be replaced with 1.6 E-6.

No.	Location	Error
77	**p. 54, Att #18**	**The old MBC Q* was used to determine the cancer exposure value of 7.59 E-7. The value should be replaced with 4.7 E-7.**

ERROR COMMENTS ON SECTION C
Thiophanate-methyl - REVISED Report of the Hazard Identification Assessment Review Committee, dated December 16, 1999

No.	Location	Error
1	**p. 8, ¶ 3**	**Add the words "4-hr" inside the parentheses giving the LC50. Line 4: add hyphen to thiophanate-methyl.**
2	**p. 12, ¶ 2**	**This paragraph refers to "acceptable studies" which "do not satisfy" the guidelines. This discrepancy must be corrected. In each case on this page the referenced studies are Acceptable and satisfying the guidelines.**
3	**p. 12**	**There is no reference to MRID 41608910, a mutagenicity study submitted by Elf Atochem.**
4	**p. 13, ¶ 3, line 8**	**EPA states: "Since it is generally acknowledged that somatic cell aneuploidy may be involved in carcinogenesis and the test article caused morphologically transformed cells in vitro, it is not surprising that the results from genetic toxicology testing with thiophanate-methyl correlate favorable with the data from the chronic feeding study demonstrating hepatocellular carcinomas in male and female mice (MRID 42607701)." This statement is incorrect. The referenced feeding study established that thiophanate-methyl did not induce hepatocellular carcinomas in either male or female mice. Thus there is no correlation.**

5	**p. 13, ¶ 3, line 14**	**Error in the Agency's conclusion that "the possible role of Thiophanate-methyl in contributing to birth defects cannot be determined at this time since both rats developmental toxicity studies were considered unacceptable"** **We disagree with the Agency's conclusion for the following reasons:** • **The Agency conclusion "...contributing to birth defects cannot be determined"contradicted the Agency's own statement on page 13 ¶ 3 line 15, which said "There was, however, no indication of a developmental effect in these studies".** • **We disagree that both rat studies were unacceptable. The first rat study (MRID 00106090) was re-classified as Unacceptable/Upgradable not based on scientific merits but rather on inadequate information on the test material, data which have no impact whatsoever on the validity of the results. There were no developmental toxic effects in this first study. The second rat study (MRID 00146643) was classified by the Agency as Acceptable-Non Guideline with no developmental toxic effects noted. The second study was classified as Non-guideline due to the selection of the dietary route of administration (discussed below) and not unacceptable.** • **Collectively, data from both studies support the lack of developmental toxicity with thiophanate-methyl in the rat.**
6	**p. 14, ¶ 2, line 3**	**Thiophanate-methyl is misspelled.**

7	**p. 16, ¶ 3; p. 23, Section VII**	**We disagree that the a data gap exists for developmental toxicity in rats for the following reasons:** • **The first rat study by gavage (MRID 00106090) was initially classified as Core Minimum then re-classified as Unacceptable/Upgradable by HIARC. The study was upgradable since the results were scientifically valid and some data on the test material were missing. The missing information had no impact on the outcomes of the study. The data still support the lack of developmental toxicity in this study..** • **The second rat study (MRID 00146643) was classified by the Agency as Acceptable but Non-guideline since the dietary route of administration was used instead of gavage. Although we recognize the limitations of dietary vs. gavage administration, we disagree with the Agency's classification since the dietary route of administration was selected at the request of the Agency and this repeat study was initiated to satisfy the Agency's demand (memo of R. Gardner, 5/22/85).** • **The results from both rat studies were scientifically valid with no developmental toxic effects noted at any of the doses tested. Using the weight of evidence approach, the data strongly endorse the lack of developmental toxicity with thiophanate-methyl in the rat.** • **The Agency has concluded that "there was no indication of developmental toxicity in those studies" [page 13, ¶ 3, line 15], so repeating a study just to satisfy the guidelines without consideration of the negative results noted in both studies is unjustified scientifically and humanely. We trust that §83-3 (a) Subdivision F guidelines has been satisfied using the weight of evidence approach.**
8	**p. 17, ¶ 3, line 3**	**Thiophanate-methyl is misspelled.**

9	**p. 17, ¶ 5**	**Error in the establishment of the developmental toxicity NOAEL from the rabbit developmental toxicity study (MRID 40022801) The Agency indicated that "the developmental toxicity LOAEL is 6 mg/kg/d based on increased fetal and litter incidence of asymmetric pelvis. The NOAEL is 2 mg/kg/d."** **We believe that the establishment of the developmental toxicity NOAEL at 2 mg/kg/day on the basis of asymmetric pelvis was incorrect because:** • **Although the fetal and litter incidence of asymmetric pelvis were increased, there were no statistical differences at any of the doses tested (2, 6 and 20 mg/kg/d) in the referenced study (LSR 1986 - MRID 40022801).** • **All other skeletal variations noted in this study were also not statistically significant from controls and were of "uncertain toxicological significance" as indicated by the EPA reviewer.** • **The findings of asymmetric pelvis were of uncertain toxicological significance and were not detrimental to the fetuses as evidenced by the lack of effects on fetal weight and litter size.** • **A weight of evidence approach was not taken by the Agency when evaluating the developmental toxicity potential of Thiophanate-methyl. Data from a second developmental toxicity in rabbits (Argus, 1997 - MRID No. 45051001) that was submitted to the Agency were not included in the HIARC evaluation.** **We believe that the developmental toxicity NOAEL of Thiophanate-methyl in rabbits should be established at 20 mg/kg/d because:** • **In the first study ((LSR 1986 - MRID 40022801) the 20 mg/kg/d dosage level (highest dose tested) was not associated with either statistically or biologically significant findings.** • **In the repeat study (Argus, 1997 - MRID No. 45051001), no developmental toxic effects were noted at the 20 mg/kg/d dosage level.** • **Collectively, the data strongly support a developmental toxicity NOAEL of Thiophanate-methyl in rabbits at 20 mg/kg/day.**

10	**p. 18, ¶ 1, line 2**	**There is a reference to MRIDs 42899101 "to -05". We have checked the NPIRS database and 42899102 - 05 do not exist.**
11	**p. 18, ¶ 2**	**We disagree with the Agency establishment of the systemic NOEL from the two-generation reproduction study at <200 ppm (13.7 mg/kg/day) for the following reasons:** **• Increased organ weights correlated with statistically increases in hepatocellular hypertrophy and thyroid follicular cell hyperplasia/hypertrophy were noted only at the highest dose tested (2000 ppm). The incidences in the mid (630 ppm) and lowest doses tested (200 ppm) were not statistically different and the effects were slight to minimal, a fact recognized by the EPA reviewer (page 18, 2nd paragraph)** **• Since the effects at the 200 ppm were not statistically different and were minimal and were less in the succeeding generation, the 200 ppm dosage level should be considered as the NOAEL and not as the LOAEL. Even the EPA reviewer indicated that "this LOAEL is considered to be a bordeline NOAEL/LOAEL" (page 18, 2nd paragraph)**
12	**p. 19, ¶ 6, line 4**	**There is a reference to MRIDs 42899101 "to -05". We have checked the NPIRS database and 42899102 - 05 do not exist.**
13	**p. 20, ¶ 2, line 2**	**There is a reference to MRIDs 42899101 "to -05". We have checked the NPIRS database and 42899102 - 05 do not exist.**

14	**pp. 19, 20**	**<u>Determination of Susceptibility</u>** **We disagree with the Agency's conclusion that the data provided evidence of increased susceptibility as evidenced by a developmental toxicity NOAEL of 2 mg/kg/d compared to a maternal toxicity NOAEL of 6 mg/kg/d for the following reasons:** • **A weight of evidence approach was not taken by the Agency. Results from the repeat rabbit developmental toxicity study (Argus 1997 - MRID No. 45051001) were not considered by the Agency. No evidence of increased susceptibility was noted in the repeat study, in which the developmental toxicity NOAEL is greater that the maternal toxicity NOAEL.** • **In the original study (LSR England, 1986), the developmental toxicity NOAEL should be 20 mg/kg/d and not 2 mg/kg/d as erroneously established by the Agency. A developmental toxicity NOAEL of 20 mg/kg/d compared to a maternal NOAEL of 6 mg/kg/d would indicate that thiophanate-methyl was not a developmental toxicant in rabbits.** • **Although the rat developmental toxicity studies were currently classified by the Agency as Unacceptable/Upgradable, the results nevertheless did not show evidence of increased susceptibility. In fact, no developmental toxic effects whatsoever were noted in both rat studies.** • **The available data support the lack of developmental toxicity in two species.**

15	**several**	**Error in the use of the developmental toxicity NOAEL of 2 mg/kg/d in the assessment of (1) acute RfD for subpopulation Females 13+ [page 3], (2) chronic RfD for subpopulation Females 13+ [page 5], (3) short and intermediate term dermal [page 7], (4) long term dermal [page 7], and (5) inhalation exposure [page 8]** **As indicated on our responses above, we believe that the establishment of the developmental toxicity NOAEL at 2 mg/kg/day was erroneous. Based upon the lack of statistical and biological differences, the lack of reproducibility of the effects, the lack of consideration of additional data from the second rabbit developmental toxicity study, and the lack of developmental effects noted in the second rabbit study even at higher dosage levels, the developmental toxicity NOAEL in the rabbit should be 20 mg/kg/day. This NOAEL should be used in the risk assessment for (1) acute RfD for females 13+, (2) chronic RfD for females 13+, (3) short and intermediate term dermal, (4) long term dermal, and (5) inhalation exposure.**
16	**p. 20, ¶ 4**	**We disagree with the HIARC's evidence of increased sensitivity based on comparison of developmental toxicity NOAEL and maternal toxicity NOAEL. As mentioned earlier, we believe that the rabbit developmental toxicity NOAEL should be established at 20 mg/kg/d and not at 2 mg/kg/d. The new developmental toxicity NOAEL would thus be higher than the maternal NOAEL of 6 mg/kg/day.** **We disagree with HIARC interpretation that the axial skeletal variations were "possibly treatment-related". The skeletal variations noted at 6 and 20 mg/kg/d were not statistically different from concurrent controls and were within the historical control range. Therefore, these findings were correctly considered as non treatment-related by the DER reviewer.**
17	**p. 24, ¶ 2, line 10**	**Add a hyphen to thiophanate-methyl.**

18	**p. 24, Section VIII**	**Error in the request for a 90-day inhalation study.** **We agree that an inhalation study is needed for inhalation exposure risk assessment but disagree with the Agency on the type of the study. We believe that in light of the current use patterns and labeled application rates of thiophanate-methyl, a 21-day inhalation study would provide sufficient data for the Agency to conduct risk assessment via inhalation.**

ERROR COMMENTS ON SECTION D Drinking Water Assessment for Thiophanate-Methyl, dated September 21, 1999, DP Barcode D259653

No.	Location	Error
1	p. 1, ¶ 1	In the environment, thiophanate-methyl may also degrade by routes that do not require intermediate formation of MBC. Formation of MBC from thiophanate-methyl requires an intramolecular reaction that creates the benzimidazole ring, common to MBC. Thiophanate-methyl has carbamate and thiocarbamate linkages that may be cleaved by nucleophilic attack, providing opportunity for further degradation through routes alternative to MBC. For example, strawberry and turf DFR studies demonstrate rapid degradation of thiophanate-methyl; however, very little MBC is formed. As MBC is not prone to photolytic degradation or any other rapid degradation processes, it is reasonable to conclude that the majority of parent compound does not degrade through the MBC pathway. As such any assessment of surface water contamination by MBC based on the degradation of thiophanate-methyl should take into account the fact that photolytic degradation yields little MBC. The EPA's assessment of MBC drinking water risk for surface water from thiophanate-methyl application does not take into account this phenomenon.
2	p. 2, ¶ 5, last line	"la" should be changed to "lb"
3	p. 2, Conclusions¶ 1	Thiophanate-methyl and benomyl have comparable activity spectrums and would not be used on the same plot, unless the two chemical were alternated in a spray regime. In this instance, the total amount of each product would be reduced.
4	p. 2, Conclusions¶ 2	HED has concluded that DX-105 and FH-432, thiophanate-methyl related degradates, are not compounds of toxicological significance. These compounds only occur at low concentrations; therefore they are not included in the residue expression.

No.	Location	Error
5	**p. 2, Conclusions ¶ 3**	**EPA has assumed that 82.7% of thiophanate-methyl degrades to MBC based on an aerobic soil degradation study that was conducted in the dark. The soil EPA has chosen was one of several and represents a worst case assessment. More importantly, in the environment, thiophanate-methyl may also degrade by routes that do not require intermediate formation of MBC. Formation of MBC from thiophanate-methyl requires an intramolecular reaction that creates the benzimidazole ring, common to MBC. Thiophanate-methyl has carbamate and thiocarbamate linkages that may be cleaved by nucleophilic attack, providing opportunity for further degradation through routes alternative to MBC. For example, strawberry and turf DFR studies demonstrate rapid degradation of thiophanate-methyl; however, very little MBC is formed. As MBC is not prone to photolytic degradation or any other rapid degradation processes, it is reasonable to conclude that the majority of parent compound does not degrade through the MBC pathway. As such any assessment of surface water contamination by MBC based on the degradation of thiophanate-methyl should take into account the fact that photolytic degradation yields little MBC. The EPA's assessment of MBC drinking water risk for surface water from thiophanate-methyl application does not take into account this phenomenon.**
6	**p. 2, Conclusions ¶ 4**	**GENEEC is a crude model compared to PRZM-EXAMS. Risk assessments using this model are very much exaggerated for several reasons.**
7	**p. 3, ¶ 2, line 3**	**Reference to the benomyl studies in rice should be deleted from this science chapter for thiophanate-methyl . Elf Atochem does not have a registered use on rice for thiophanate-methyl and the data are not relevant to this review.**

No.	Location	Error
8	**p. 3, Environmental Fate; ¶ 1, line 1**	**EPA has assumed that 82.7% of thiophanate-methyl degrades to MBC based on an aerobic soil degradation study that was conducted in the dark. The soil EPA has chosen was one of several and represents a worst case assessment. More importantly, in the environment, thiophanate-methyl may also degrade by routes that do not require intermediate formation of MBC. Formation of MBC from thiophanate-methyl requires an intramolecular reaction that creates the benzimidazole ring, common to MBC. Thiophanate-methyl has carbamate and thiocarbamate linkages that may be cleaved by nucleophilic attack, providing opportunity for further degradation through routes alternative to MBC. For example, strawberry and turf DFR studies demonstrate rapid degradation of thiophanate-methyl; however, very little MBC is formed. As MBC is not prone to photolytic degradation or any other rapid degradation processes, it is reasonable to conclude that the majority of parent compound does not degrade through the MBC pathway. As such any assessment of surface water contamination by MBC based on the degradation of thiophanate-methyl should take into account the fact that photolytic degradation yields little MBC. The EPA's assessment of MBC drinking water risk for surface water from thiophanate-methyl application does not take into account this phenomenon.**
9	**p. 3, ¶ 3**	**Remove "A" from the beginning of the sentence.**
10	**p. 3, ¶ 5, line 2**	**Carbendazim is misspelled.**
11	**Top of page 4**	**The four MBC field dissipation references should be removed from the list. This data is only relevant to DuPont's benomyl as DuPont has proposed to use MBC to describe the fate of its parent compound. This is not the case for Topsin M. Elf Atochem has submitted field dissipation studies for our parent compound. We do not believe that MBC field dissipation half lives are being used as input parameters for the SCI-GROW, GENEEC, or PRZM/EXAMS models. Further, if MBC field dissipation half-lives are needed for thiophanate-methyl use, those parameters can be calculated from the TM field dissipation studies. That has already been conducted by Elf Atochem and can be submitted at the request of the EPA.**

No.	Location	Error
12	**p. 4, ¶ 2, line 7**	**The reference to DuPont's acceptable mobility studies (soil column leaching) should be removed. Results from these studies were not used within any of the EPA's models. The study is not required, as apparently DuPont has submitted an acceptable adsorption/desorption study.**
13	**p. 4, ¶ 2, line 21**	**The reference to MBC field dissipation should be removed. This data is only relevant to DuPont's benomyl as DuPont has proposed to use MBC to describe the fate of its parent compound. This is not the case for Topsin M. We have field dissipation studies for our parent compound. We do not believe that MBC field dissipation half lives are being used as input parameters for the SCI-GROW, GENEEC, or PRZM/EXAMS models. Further, if MBC field dissipation half-lives are needed for Topsin M use, those parameters can be calculated from the TM field dissipation studies. That has already been conducted by Elf Atochem and will be submitted.**
14	**p. 5, ¶ 1**	**Note that EPA has waived the requirement to conduct a bioaccumulation study on thiophanate-methyl.**

No.	Location	Error
15	**p. 5, Ground-water; ¶ 3, line 2**	**EPA has assumed that 82.7% of thiophanate-methyl degrades to MBC based on an aerobic soil degradation study that was conducted in the dark. The soil EPA has chosen was one of several and represents a worst case assessment. More importantly, in the environment, thiophanate-methyl may also degrade by routes that do not require intermediate formation of MBC. Formation of MBC from thiophanate-methyl requires an intramolecular reaction that creates the benzimidazole ring, common to MBC. Thiophanate-methyl has carbamate and thiocarbamate linkages that may be cleaved by nucleophilic attack, providing opportunity for further degradation through routes alternative to MBC. For example, strawberry and turf DFR studies demonstrate rapid degradation of thiophanate-methyl; however, very little MBC is formed. As MBC is not prone to photolytic degradation or any other rapid degradation processes, it is reasonable to conclude that the majority of parent compound does not degrade through the MBC pathway. As such any assessment of surface water contamination by MBC based on the degradation of thiophanate-methyl should take into account the fact that photolytic degradation yields little MBC. The EPA's assessment of MBC drinking water risk for surface water from thiophanate-methyl application does not take into account this phenomenon.**
16	**p. 6, ¶ 2, line 3**	**The use areas of TM and benomyl do coincide as their registrations overlap on a number of agricultural crops. A word is missing from the sentence "...any data show that...".**
17	**p. 7, last row**	**This scenario uses aerial application to turf. To our knowledge, in a turf and ornamentals situation (as opposed to sod farms, which are agricultural), there is no aerial application to turf. The term 'aerial' used in some of the turf and ornamental labels, refers to a type of drip spray ground-based usage.**
18	**p. 9, table 4**	**The high apple rate used here does not appear on any currently valid label. It should not be included.**
19	**p. 10, chart**	**The table lists information for wheat grown in North Dakota. Please note that TM is only registered for use on wheat in Idaho, Oregon, and Washington.**

ERROR COMMENTS
SECTION E
THIOPHANATE-METHYL HED Product Chemistry and Residue Chemistry Chapters of the RED, dated June 16, 2000, DP Barcode 230335

PRODUCT CHEMISTRY SECTION

No.	Location	Error
1	p. 1, ¶ 1, line 2	This summary shows thiophanate-methyl registered on 'forest' plantings. TM is registered for use on ornamental trees and has no registered 'forestry' uses.
2	p. 1, Section titled "Identification of Active Ingredient"	The melting point of pure thiophanate-methyl is listed here as 168°C. Although this value is certainly within the range of published values for thiophanate-methyl it appears that this value was not supplied by Atochem. We therefore cannot verify its origin or accuracy. Elf Atochem lists the melting point as 163C.
3	p. 1, Section titled "Manufacturing- use Products	The nominal AI content of thiophanate-methyl (Topsin) technical listed in the RED is 94.3% w/w. This value was apparently obtained from an obsolete Confidential Statement of Formula (CSF) and is not the current value that should be listed in our registration with the Agency. In a letter sent to the EPA dated December 4, 1996 Elf Atochem submitted a revised CSF. The CSF was approved (DF Barcode No. D232392, Reg./File Symbol No. 4581-280) February 4, 1997. This revised CSF lists the nominal value for dimethyl[(1,2-phenylene)bis(iminocarbonothioyl)]bis [carbamate] (thiophanate methyl) as being 97.0 % w/w. In addition the *Thiophanate-methyl - Preliminary Analysis of Product Samples* report which is MRID 41608901 has an eight batch average of 96.7 % w/w for the thiophanate-methyl concentration. This data clearly supports our claim of 97.0 % w/w on our current CSF.

No.	Location	Error
4	**Product Chemistry Data Summary Table, Guidelines 830.1550 & 830.1750**	**The RED indicates that information is needed on the identity, nominal concentration and purpose of each component in thiophanate-methyl technical and Certification of Ingredient Limits and that the product label claim does not fall within the certified limits. However, as we have pointed out the reviewer was apparently in possession of an obsolete CSF. The December 4, 1996 CSF for thiophanate-methyl technical, which was accepted by the Agency, indicates the identity, nominal concentration, and purpose of each component and should satisfy the data requirements for 830.1550 - Product Identity and Composition. Also the certified limits are presented in the current CSF which would fulfill the requirements for 830.1750 - Certified Limits. These limits do indeed bracket our label claim. It needs to be clarified with the Agency whether the current (1996) CSF does indeed adequately meet these requirements or if the agency will still need additional information.**

RESIDUE CHEMISTRY SECTION

No.	Location	Error
1	**p. 2, ¶ 2, line 1**	**We have seen no evidence to suggest that 2-aminobenizimidazole (2-AB) should be considered a residue of concern.**
2	**p. 4; ¶ 4;**	**Line 3: available residue data (MRID 44184301) supports 14-day PHI for succulent beans.** **Line 4: EPA has approved a 28-day PHI for dry beans.** **Line 4: Elf Atochem conducted a residue study with ten trials on dry beans that had a use pattern tied to the growth stage of the plant (1st application at 100% bloom and 2nd application 7 days later) BR-90-39 (MRID 44161001). This label ensures that the chemical compound is applied at the appropriate growth stage to ensure disease control. Most of the trials were harvested at a PHI of less than 60 days.** **Only 1 of the trials, had samples with TM or MBC residues above the LOQ at 0.05 ppm. This was a Michigan trial which had no quantifiable residues of TM , but MBC residues at 0.08 ppm. It should be noted that another trial in MI had no quantifiable residues of TM or MBC, but 0.07 ppm DX-105. That result was probably due to an interference because DX-105 residues are anticipated to be much lower than TM or MBC residues based on other residue studies and metabolism studies. A Colorado residue trial with the shortest PHI (27 days), had no quantifiable residues of TM or MBC, while the Michigan trial with 0.08 ppm MBC had a 38 day PHI.**
3	**p. 4, ¶ 5**	**Line 2: the label directions for strawberries have already been revised to indicate a maximum rate/season.**
4	**p. 5, ¶ 4, line 2**	**Elf Atochem is now preparing for submission in October a field rotational crop study at two sites. There are no measurable residues in any of the rotated crops 30 days after the last application to the target crop.** **Line 3: directions on sugarcane have been removed from the labels.**
5	**p. 5, ¶ 6**	**Line 4:We have seen no evidence to suggest that 2-aminobenimidazole (2-AB) should be considered a residue of concern.**
6	**p. 6, ¶ 4, line 20**	**As part of the plant enforcement method submission, the Elf Atochem submitted a successful independent laboratory validation (ILV) study (MRID 44703602).**

No.	Location	Error
7	**p. 7, ¶ 3, line 1**	**Elf Atochem has submitted an animal commodities' enforcement method for TM and provided a successful ILV study. (MRID 44526101)**
8	**p. 7, ¶ 6,**	**Line 3: No storage stability studies on MBC are required. On June 18, 1996, EPA met with Elf Atochem to determine what storage stability data would be required to support studies being submitted at that time. At the meeting, the Agency stated that submitted storage stability studies demonstrated that MBC was highly stable when stored frozen and that this data could be extrapolated up to 5 years demonstrating satisfactory stability of MBC. On this basis, the EPA stated that no additional residue data was required for MBC. Interim reports for thiophanate-methyl have been submitted to the EPA on a 6 month basis for the past several years, in accordance with the Agency's decision that only storage stability data would be required for the parent compound.** **Line 5: Because the EPA has agreed to use plant metabolism studies as a basis for calculating the level of 2-AB residues in crop samples, there should be no requirement for developing 2-AB storage stability data. Should Elf Atochem develop residue data for 2-AB at some point in the future, storage stability studies for 2-AB would be generated.**
9	**p. 7, ¶ 7**	**Note that MBC storage stability was submitted for snap beans, apples, wheat grain, spinach, sugarbeet roots, and tomatoes. TM storage stability covers apples, wheat grain, cucumbers, snap beans, sugarbeets, and soybeans. In some cases, results up to 36 months have been submitted.**
10	**p. 7, ¶ 8, line 1**	**Elf Atochem has submitted storage stability data for thiophanate-methyl MBC, and the other minor metabolites in animal commodities that demonstrates stability to support all samples analyzed for milk and tissues (MRID 44592301). Although some data for the minor metabolites have been submitted, the EPA has agreed to use animal metabolism studies as a basis for calculating the level of 4-OH-MBC, 5-OH-MBC, and 5-OH-MBC-S residues in animal commodity samples, therefore there should be no requirement for developing storage stability data for these metabolites.**
11	**p. 8, ¶ 3, line 3**	**The following residue studies have been submitted to EPA: almond, dry pea, peanut, pecan, potato, soybeans, sugar beet.**

No.	Location	Error
12	**p. 8, ¶ 4, line 3**	**TM storage stability data that can be translated for beans (dry and succulent) and peaches/nectarines have been submitted as part of our ongoing storage stability program.**
13	**p. 8, ¶ 5, line 1**	**The following residue studies have been submitted to EPA: almond, dry pea, peanut, pecan, potato, soybeans, sugar beet.**
14	**p. 8, last line**	**If the reregistration requirements for magnitude of the residue in plants are fulfilled (same page, ¶ 3), then no further trials should be required.**
15	**p. 9, ¶ 2**	**Line 4: ILV studies have been conducted and submitted to EPA. We believe only radiovalidation work remains to satisfy this requirement.** **Line 6: TM storage stability data that can be translated for grapes have been submitted as part of our ongoing storage stability program. The 3 required residue studies have been completed and will be submitted.**
16	**p. 9, ¶ 3, line 6**	**The following processing studies have been submitted to EPA:** **peanut (MRID 44850901)** **potato (MRID 44498502)** **soybean (MRID 44582702)** **sugar beet (MRIDs 44643502, 44584601)**
17	**p. 11, ¶ 2, line 1**	**Storage stability data for animal commodities has been submitted to EPA and should be considered within this RED chapter.**
18	**p. 14, Beans**	**Note that the following use pattern has been approved by EPA:** **Apply 1-2 lbs (product) per acre per application** **Make first application when 10% to 30% of plants have at least one open bloom, and/or conditions are favorable for disease development. A maximum of 4 lbs product per acre (2.8 lbs ai) per crop cycle may be used, with a 4-7 day spray interval. PHI, CA only: 14 days for snap beans, 28 days for lima and dry beans. PHI, all other states: 14 days for snap and lima beans, 28 days for dry beans.**
19	**p. 15, Cucurbits**	**EPA recently approved application by underground drip irrigation.**

No.	Location	Error
20	**p. 19**	**The following changes should be made on this page's listings: Potatoes: the MRID 44468201 listed here is actually for a watermelon study. Add to Nature of the Residue Livestock: MRID 43019201. Add to Analytical Methods: animal ILV MRID 44523101, plant ILV MRID 44703602 Note that registrations on celery have been cancelled.**
21	**p. 20**	**The following changes should be made: Beans, snap: the MRID 44083802 listed here is actually for lima beans. Add to soybeans: MRID 44572701.**
22	**p. 21**	**The following changes should be made: Melons: add MRID 44468201 (watermelon) Almonds: add MRID 44487001 Pecans: add MRID 44498501 Wheat: add MRID 44106901**
23	**p. 22**	**The following changes should be made: Peanuts: add MRID 44515701 Processed peanuts: add MRID 44850901 Processed potato: add MRID 44498502 Processed soybean: add MRID 44572702 Processed sugarbeet: add MRID 44584601 860.1480 MMPE: add MRID 44592301, 44287501**
24	**p. 23**	**Footnote 13: 'enforcement' is misspelled. Also change to refer to the fact that ILV studies have been submitted.**

No.	Location	Error
25	**p. 24**	**Footnote 18: No storage stability studies on MBC are required. On June 18, 1996, EPA met with Elf Atochem to determine what storage stability data would be required to support studies being submitted at that time. At the meeting, the Agency stated that submitted storage stability studies demonstrated that MBC was highly stable when stored frozen and that this data could be extrapolated up to 5 years demonstrating satisfactory stability of MBC. On this basis, the EPA stated that no additional residue data was required for MBC. Interim reports for thiophanate-methyl have been submitted to the EPA on a 6 month basis in accordance with the Agency's decision that only storage stability data would be required for the parent compound.** **Because the EPA has agreed to use plant metabolism studies as a basis for calculating the level of 2-AB residues in crop samples, there should be no requirement for developing 2-AB storage stability data. Should Elf Atochem develop residue data for 2-AB at some point in the future, storage stability studies for 2-AB would be generated.** **Footnote 24: EPA states that for a submitted sugar beet residue study, one of the two California trials failed due to poor quality of the RAC. We believe that the remaining data which includes eleven successful residue trials should be sufficient to support this use.** **The sugar beet top sample in question had a residue value of greater than 15 ppm; whereas the next highest trial was in 1.6 ppm TM and 3.1 ppm MBC or 4.7 ppm total TM based residues which is 1/3 the level of the current tolerance. It should also be pointed out sugar beet tops was only assumed to be 10% of the dairy cow diet by the EPA; thus the sugar beet tolerance has little bearing on the dietary risk assessment. Residues in meat and milk are very low at all feeding levels.** **Footnote 28: EPA has accepted a label change to a 28-day PHI for dry beans.**
26	**p. 25**	**Footnote 30: change to note that soybean RAC studies have been submitted.**

No.	Location	Error
27	**Pg. 26**	**Footnote 41: change to note that almond residue studies have been submitted.** **Footnote 42: change to note that pecan residue studies have been submitted.** **Footnote 44: EPA states that the method recoveries for forage, hay, straw were unacceptable; however recoveries for MBC were well within EPA's acceptable range and recoveries of TM were 71% for forage, 66% for hay, and 71% for straw. Two of the commodities have an average recovery within EPA specifications of 70 - 120% and one commodity is just slightly outside of this range. Some residue were seen in control samples; however results were appropriately corrected for the noted contamination. It should also be pointed out of all the wheat feedstocks, only the grain itself was used in EPA's calculation of the burden to cattle and dairy cows; thus the forage, hay, and straw tolerance has no bearing on the dietary risk assessment. Residues in meat and milk are very low at all feeding levels.** **Footnote 47: change to note that peanut residue studies have been submitted.** **Footnote 50: change to note that processing studies for peanut, potato, soybean, and sugar beet have been submitted.**
28	**p, 27**	**Footnote 51: change to note that storage stability data for animal commodities have been submitted.**
29	**p. 28, ¶ 7**	**"Additional data" - this list includes the following crops which elsewhere say "no additional data required" (see pg. 21): cucumbers, melons, pumpkins, squash. It also includes the following, for which residue data have been submitted: almonds/hulls, pecans, potatoes, peanuts, soybeans, sugarbeets, and wheat. This leaves only green onions.**
30	**p. 28, ¶ 8, last line**	**Please note that the high residue value listed for cherries is from a trial which was not performed according to commercial practice.**
31	**p. 29, ¶ 3, line 4**	**The combined residues of MBC in whole milk was 0.034 ppm TM equivalents and for skim milk 0.044 ppm. Tolerance should be established as 0.1 ppm, not 0.15 ppm.**
32	**p. 29, ¶ 3, line 6**	**The combined residues of TM and MBC in muscle, fat, and liver was <0.045 ppm TM equivalents and <0.075 ppm in kidneys. Tolerance should be established at 0.1 ppm, not 0.15 ppm.**

No.	Location	Error
33	**p. 30, 31, 32: Table C**	**Revise to include the RAC and processing studies which have in fact been submitted. Revise <u>bananas</u> to indicate not that Registrant is not supporting, but that additional trials are required. Also revise to note that <u>celery</u> was cancelled, not 'unsupported'. <u>Cherries</u> will not require an increase in tolerance, since the high residue values came from trials not done according to commercial practice (as noted in the study). <u>Pumpkins</u> say that additional data are required, while p. 21 of this document says no data are required. <u>Sugarcane</u> use is not 'unsupported', it is cancelled.**

ERROR COMMENTS
SECTION F
THIOPHANATE-METHYL CASE #2680 Revised Toxicology Chapter for the Reregistration Eligibility Decision Document, dated December 21, 1999, DP Barcode D261951

No.	Location	Error
1	**General**	**There are two sections 3.1.5: the first is on page 17 for Neurotoxicity and the second is on page 18 for Genotoxicity.**
2	**p. 2, ¶ 1 Section 3.1.1**	**The Agency's rationale for requesting additional mutagenicity studies is in error because** **• The Agency has confirmed that thiophanate-methyl is an "inducer of aneuploidy" and "the acceptable studies submitted to the Agency combined with the data from the open literature studies satisfy the mutagenicity test guidelines, and that no further testing is warranted" [page 11 and 12 of HIARC report].** **• Requesting additional mutagenicity studies to resolve the equivocal results and to assess the direct mutagenic potential of thiophanate-methyl is a moot point since the chemical has already been characterized as an aneugen by the Agency.** **• The requested mutagenicity studies would not serve any regulatory needs.** **• The requested gene mutation study for the metabolite 2-aminobenzimidazole is also unnecessary since this metabolite would not change the classification of thiophanate-methyl as an aneugen. Furthermore, the conversion of thiophanate-methyl to this metabolite is negligible.**
3	**p. 3, ¶ 4**	**The Agency recommended a dermal absorption rate of 7%. While we previously agreed with the Agency's determination, a recently received dermal absorption study using human skin reveals a rate of 0.07% for the neat material. This study will be submitted to the Agency as soon as possible.**

No.	Location	Error
4	**p. 4**	**The section on guideline 82-1a should include MRID 42533802. Right column should say 'decreased thymus weight', not increased thymus weight. The section on guideline 82-1b has an incorrect MRID: 42311801 should be changed to 41982203.**
5	**p. 5 2nd row, right column**	**There is a discrepancy as follows. The table states: "Increased incidence of hepatocellular adenomas in males at > 467.6 mg/kg/day (control to high dose, 9%, 17%, 15%, 42% and 57%[a]) and in females at > 123.3 mg/kg/day (0%, 0%, 8%, 24% and 56% [a]). Both sexes showed significant increasing trends and pairwise increases at the highest two dose levels." There appears to be a contradiction between the incidences for hepatocellular adenomas cited above and the values expressed on page 10 of this document, under "Discussion of Tumor Data" (and also on page 11 of the Revised Report of the Hazard Identification Assessment Review Committee, 12/16/99), i.e., "The incidence of hepatocellular adenoma was increased (statistically significant, p<0.01) in both males and females at 3000 and 7000 ppm, the highest two dose levels tested. From control to high dose, the incidence was 7%, 13%, 12%, 32% and 40% in males and 0%, 0%, 5%, 13% and 30% in females." (emphasis added) The incidences were thus different from those listed on Table 1. The reasons for these differences should be explained.**
6	**p. 6, ¶ 1 line 2**	**The word 'topsin' should be changed to thiophanate-methyl.**

No.	Location	Error
7	**p. 7, bottom ¶, line 10 to end of ¶**	**Corrections or clarifications are needed as follows.** **1. The reference to dosage levels of 153.0 mg/kg/day for females or 393.6 mg/kg/day for either sex in the CD-1 mouse study is not compatible with other statements in this document. For instance, on page 90 of the HED preliminary risk assessment, the consumption levels are given as 0, 23.7, 98.6, 467.6, or 1078.8 mg/kg/day (males), and 0, 28.7, 123.3, 557.9, or 1329.4 mg/kg/day (females), and these dosage levels are consistent with the data presented in the final study report (MRID 42607701).** **2. While technically correct, it is confusing and perhaps misleading to state that "the combined incidence of adenoma and carcinoma was also increased in males, but the incidence of carcinomas was not increased." Since the incidence of carcinomas was not increased in males, it is obvious that the increase in incidence of combined adenomas and carcinomas is due solely to the increased incidence of adenomas. It would be clearer to discuss the incidence of carcinoma per se, e.g. the incidence of carcinomas was not increased in males and there were no carcinomas found in females. If combined incidences of adenomas and carcinomas are also to be discussed, then a rationale should first be presented as to the reason for combining these two tumor types.** **3. It is inappropriate to state that incidences were above the available historical control data. In fact, only adenomas were found in excess. Carcinoma incidence was within the bounds of historical controls.**

No.	Location	Error
8	**p. 8, ¶ 2**	**EPA states: "A Q_1* of 2.08 x 10^{-1} (mg/kg/day)$^{-1}$ was assigned based on the dose-dependent increases in liver tumors in male and female mice (quantitative risk assessment memorandum from L. Brunsman to N. McCarroll and L. Hansen dated April 6, 1999)"** **This discussion must be updated. The Q_1* (mg/kg/day)$^{-1}$ values for mouse liver tumors were revised downward to 1.38 x 10^{-2} (males) and 6.7 x 10^{-3} (females), as per the memorandum from L. Brunsman to N. McCarroll dated March 16, 2000. As noted in our comments on the revised quantitative risk assessment, however, even these potency estimates remain overstated. The relevance of mouse liver tumors to human risk assessment is highly questionable. If quantitative risk assessment is to be applied, case-specific (rather than default) values should be used for these calculations.**
9	**p. 8, ¶ 2**	**EPA states: "The thyroid tumors in rats were also considered treatment-related because a dose-dependent increase was observed in both sexes (in males, toxicity at the HDT was excessive based on high mortality but the tumors were nonetheless considered treatment-related)."** **The results of the study indicate that toxicity in both sexes was excessive at the highest does tested; therefore, we respectfully note that it is inappropriate to use the data from this group for risk assessment purposes.**

No.	Location	Error
10	**p. 9**	**In the section called <u>Adequacy of the Dose Levels Tested</u>, it should be noted that the high dose female group received <u>6000</u> ppm of the test material in the diet, rather than 5000 as stated. We agree with the Agency's determination that dosing was considered adequate at 1200 ppm and the MTD was exceeded at 6000 ppm in males. It should be noted, however, that the MTD was also exceeded at 6000 ppm in females, which showed a mean net body weight gain of only 69% ($p<0.001$) of the control value at the end of the study. This difference far exceeds the generally-accepted standards set for establishing the MTD at a level that produces a decrement in body weight gain $\geq$10% when compared to control values. In this study, we respectfully submit that the MTD for females was approximately 1200 ppm based on the adverse effects in multiple organs as noted above, as well as the reduction in food efficiency to 88% of control values.**
11	**p. 11 Section 3.1.4**	**We disagree with the Agency assessment that "developmental toxicity was observed in the rabbit and included asymmetric pelvis and possibly other axial skeletal abnormalities such as thickened ribs at the costal cartilage" in light of:** • **The fetal and litter incidence of asymmetric pelvis were not significantly increased at any of the doses tested (2, 6 and 20 mg/kg/d) in the referenced study (LSR 1986 - MRID 40022801).** • **All other skeletal variations noted in this study were also not statistically significant from controls and were of "uncertain toxicological significance" as indicated by the EPA reviewer.** • **The findings of asymmetric pelvis were of uncertain toxicological significance and were not detrimental to the fetuses as evidenced by the lack of effects on fetal weight and litter size.** • **A weight of evidence approach was not taken by the Agency when evaluating the developmental toxicity potential of Thiophanate-methyl in rabbits. Data from a second developmental toxicity in rabbits (Argus, 1997 - MRID No. 45051001) that was submitted to the Agency were not included in the HIARC evaluation. No developmental toxic effects were noted in this repeat study.**

No.	Location	Error
12	**p. 11 Section 3.1.4**	**We believe the Agency assessment of increased sensitivity of the offspring is in error for the following reasons:** • **A weight of evidence approach was not taken by the Agency. Results from the repeat rabbit developmental toxicity study (Argus 1997 - MRID No. 45051001) were not considered by the Agency. No evidence of increased susceptibility was noted in the repeat study, in which the developmental toxicity NOAEL is greater that the maternal toxicity NOAEL.** • **In the original study (LSR England, 1986), the developmental toxicity NOAEL should be 20 mg/kg/d and not 2 mg/kg/d as erroneously established by the Agency. A developmental toxicity NOAEL of 20 mg/kg/d compared to a maternal NOAEL of 6 mg/kg/d would indicate that thiophanate-methyl was not a developmental toxicant in rabbits** • **Although the rat developmental toxicity studies were currently classified by the Agency as Unacceptable/Upgradable, the results nevertheless did not show evidence of increased susceptibility. In fact, no developmental toxic effects whatsoever were noted in both rat studies.** • **The available data support the lack of developmental toxicity in two species.**
13	**p. 12**	**The section on guideline 83-3b should include MRID 41056701.** **The section on guideline 83-4 refers to MRIDs 42899101 "to -05". No such MRIDs were found in our data search.** **The section on guideline 83-4 should include MRID 43624401.** **¶ 1, line 2: thiophanate-methyl is misspelled.**

No.	Location	Error
14	**p. 13 Developm. Toxicity**	**We disagree with the Agency conclusion that the existing data do not fulfill the requirement for a rat developmental toxicity study for the following reasons:** • **The first rat study by gavage (MRID 00106090) was initially classified as Core Minimum then re-classified as Unacceptable/Upgradable by HIARC. The study was upgradable since the results were scientifically valid but some data on the test material were missing with the missing information having no impact on the outcomes of the study. The data support the lack of developmental toxicity in this study.** • **The second rat study (MRID 00146643) was classified by the Agency as Acceptable but Non-guideline since the dietary route of administration was used instead of gavage. Although we recognize the limitations of dietary vs. gavage administration, we disagree with the Agency's classification since the dietary route of administration was selected at the request of the Agency and this repeat study was initiated to satisfy the Agency's demand (memo of R. Gardner, 5/22/85).** • **The results from both rat studies were scientifically valid with no developmental toxic effects noted at any of the doses tested. Using the weight of evidence approach, the data strongly endorse the lack of developmental toxicity with thiophanate-methyl in the rat.** • **Since the Agency has concluded that "there was no indication of developmental toxicity in those studies", repeating a study just to satisfy the guidelines without consideration of the negative results noted in both studies is unjustified scientifically and humanely. We trust that §83-3 (a) Subdivision F guidelines has been satisfied using the weight of evidence approach.**
15	**p. 15**	**¶ 1, line 3: thiophanate is misspelled.** **Last paragraph, line 2: as noted above, MRIDs 42899102 to -05 do not exist.**

No.	Location	Error
16	**p. 15, ¶ 4**	**We believe that the establishment of the developmental toxicity NOAEL at 2 mg/kg/day on the basis of asymmetric pelvis was incorrect for the following reasons:** • **Although the fetal and litter incidence of asymmetric pelvis were increased, there were no statistical differences at any of the doses tested (2, 6 and 20 mg/kg/d) in the referenced study (LSR 1986 - MRID 40022801).** • **All other skeletal variations noted in this study were also not statistically significant from controls and were of "uncertain toxicological significance" as indicated by the EPA reviewer.** • **The findings of asymmetric pelvis were of uncertain toxicological significance and were not detrimental to the fetuses as evidenced by the lack of effects on fetal weight and litter size.** • **A weight of evidence approach was not taken by the Agency when evaluating the developmental toxicity potential of thiophanate-methyl. Data from a second developmental toxicity in rabbits (Argus, 1997 - MRID No. 45051001) that was submitted to the Agency were not included in the HIARC evaluation.** **We believe that the developmental toxicity NOAEL of Thiophanate-methyl in rabbits should be established at 20 mg/kg/d for the following reasons:** • **In the first study (LSR 1986 - MRID 40022801) the 20 mg/kg/d dosage level (highest dose tested) was not associated with neither statistically nor biologically significant findings.** • **In the repeat study (Argus, 1997 - MRID No. 45051001), no developmental toxic effects were noted at the 20 mg/kg/d dosage level.** • **Collectively, the data strongly support a developmental toxicity NOAEL of Thiophanate-methyl in rabbits at 20 mg/kg/day.**

No.	Location	Error
17	**p. 16**	**We disagree with the Agency establishment of the systemic NOEL from the two-generation reproduction study at <200 ppm (13.7 mg/kg/day) for the following reasons:** • **Increased organ weights correlated with statistical increases in hepatocellular hypertrophy and thyroid follicular cell hyperplasia/hypertrophy were noted only at the highest dose tested (2000 ppm). The incidences in the mid (630 ppm) and lowest doses tested (200 ppm) were not statistically different and the effects were slight to minimal, a fact recognized by the EPA reviewer (page 18, 2nd paragraph)** • **Since the effects at the 200 ppm were not statistically different and were minimal and were less in the succeeding generation, the 200 ppm dosage level should be considered as the NOAEL and not as the LOAEL. Even the EPA reviewer indicated that "this LOAEL is considered to be a borderline NOAEL/LOAEL" Page 16).**
18	**p. 17, ¶ 6 line 4**	**The MRIDs 42899102 to -05 do not exist.**
19	**p. 18**	**One mutagenicity test (MRID 41608910) submitted by Elf Atochem is not included in the Agency's considerations.**
20	**p. 22**	**In the doses column, first row, there is an improper line break for the superscript.**

ERROR COMMENTS ON SECTION G THIOPHANATE-METHYL: OCCUPATIONAL AND RESIDENTIAL EXPOSURE ASSESSMENT AND RECOMMENDATIONS FOR THE REREGISTRATION ELIGIBILITY DECISION DOCUMENT dated June 21, 2000, DP Barcode D264018

No.	Location	Error
1	General	US EPA relied on simple, screening-level SOPs in residential risk assessment in the absence of a validated residential exposure model. However, this screening process overestimates human outdoor residential exposure to pesticides. A fundamental error in the residential SOPs is the assumption that dermal transfer of residues to a person from the environment is linear over time. This transfer process has been proven to be readily saturable. The ORETF, of which Elf Atochem is a member, has identified and pooled results of studies conducted by ORETF, its member companies, and governmental and academic institutions. The integration of these results provide data for a more refined, but still conservative estimate of exposure on turf for adults and children. By using these data calculated exposure risk values are reduced substantially. Therefore, Elf Atochem requests that the Agency re-assess non-occupational risk using the ORETF model as a refinement of its SOPs. This will affect both residential and occupational exposure assessments, and should result in exposure reductions (and corresponding increases in MOE) of approximately two to four-fold. Estimates specifically affected will be hose end applications, drop spreader applications, and LCO spray applications. Because the ORETF data were submitted to EPA over six months ago, it is surprising that they have not been used.
2	General	The ARTF and ORETF have supplied the Agency with a broad database of transfer coefficients (Tc) for use in risk assessments. The Agency, in turn, has stated that they would use these Tc values in assessing the exposure potential for ARTF member products. None of the Tc values developed by the two task forces are used in this draft RED. The result of using ARTF Tcs will be a reduction in reentry worker exposure (and increase in MOE) by nil to four-fold. Most of the MOE will increase by at least two-fold.

No.	Location	Error
3	**General**	**Unlike the other documents comprising the draft thiophanate-methyl RED, the name of the software used to perform the various risk assessments or exposure scenarios of non-mixer/loader/applicator subjects is not included. The PHED database is cited for MLA scenarios.**
4	**General**	**EPA has used defaults values which are conservative estimates derived from general knowledge of registrant submissions to date and relevant literature. ARTF has developed exposure data on the magnitude of exposure Transfer Coefficients based on new and existing field work. Data generated and analyzed to date suggests that the defaults Tcs now used by EPA overestimate contact potentials. A few examples illustrate the impact that these new revised exposure estimates will make on the overall occupational risk calculations contained in the RED. It is recommended that ARTF database which is now available to EPA evaluators be used in occupational risk assessments.**
5	**p. 4**	**Thiophanate-methyl (TM) is described as systemic, which is not entirely accurate. A very small fraction of TM will penetrate plant tissue but its effects are mostly related to its surface activity. This distinction is not extremely relevant to the topic addressed by this document but it will have major implications on the dietary risk topic.**
6	**p. 4, ¶ 1**	**Missing footnote? This reference matches footnote 6 regarding QA analysis.**
7	**p. 4, ¶ 2**	**Missing footnote? This reference matches footnote 5, Incident Reports.**
8	**p. 4, ¶3**	**Line 3: typographical error in units following the Q* value. "../day^{-1}" is redundant. Recommend that the "$^{-1}$" be deleted. Bottom: Typographical error: "stud" should be "study".**
9	**p. 4 bottom**	**Error: change the word "only" to "do not".**
10	**p. 5 line 2**	**Error: add "on" after "based".**
11	**p. 5, main ¶**	**Several footnotes are in error: change 5 to 7. Change 6,7 to 8,9. Change 8 to 10.**

No.	Location	Error
12	p. 6 ¶ 1	Third line from bottom: a word is missing after "...for which engineering controls were...". Same line, the close parentheses do not track.
13	p. 6, ¶2	Footnotes are in error: change 9,10,11,12 to 11,12,13,14.
14	p. 6, ¶3, line 3	Elf Atochem has provided four transferrable residue studies, not three as stated in the text.
15	p. 6	Middle paragraph, line 6. The reference to "the submitted study" should be plural since 4 studies were submitted.
16	p. 7, ¶ 1, last line	Footnotes are in error: change 13,14 to 17,18.
17	p. 7, ¶1 & 2	The document states that the turf transferrable residue study provided by Elf Atochem was used as a basis for all of its turf exposure calculations but the Agency may have failed to use appropriate reduction factors for extrapolation of the data to formulations that result in lower transferrable residues than the wettable powder formulation. Data towards this effect are available from the Outdoor Reentry Exposure Task Force (ORETF) and we will try to obtain either copies of the reports or the MRIDs for the reports (in the case that these reports have already been submitted).
18	p. 7, ¶ 2	An unacceptable MOE has been calculated for a toddler orally ingesting TM-containing granules from a granular application.
19	p. 7, ¶ 3	Although the Cleary 3336F label mentions that the product may be used for control of fungal diseases in fruit trees, this use is virtually non-existent.
20	p. 7, ¶3	Line 3: add "hours" after "24". Line 7: A typo exists in the phrase "an MOE of MOE". The second MOE should be deleted. Second to last line: "a adolescent" should be "an adolescent".
21	p. 8, ¶ 1	Home/ recreational lawn applications are very distinct scenarios and should be split into at least two separate risk scenarios. Whereas some recreational scenarios (golf courses) are treated with TM, most other turf environments are not. TM is not usually used on domestic lawns except under severe fungal pressure situations. Granular application of TM via inclusions with fertilizer products (Scotts Chemical Co. products) usually occurs only once per year.

No.	Location	Error
22	**p. 8, ¶ 1**	**The assumptions used for the calculation of cancer risks are generally too conservative. Market data presented at the SMART meeting will not support these assumptions. Additional data are being submitted.**
23	**p. 8, ¶ 3**	**The document includes an error in interpretation of the "moisture" comments in the TTR and DFR studies submitted to the EPA. This document infers that the authors were alluding to such residues being washed off by rain or irrigation. While true, the authors were referring to the normal levels of relative humidity in the air at the various sites. The humidity in the air may, and probably does, hydrolyze surface-available residues of TM. The washing off effect of rain and irrigation would presumably be the same for TM as for any other wettable powder formulation sold for turf.**
24	**p. 9**	**This document lists eight studies which would allow the Agency to better estimate certain exposure scenarios. However, the document does not mention that Elf Atochem participates in both the Agricultural Reentry Task Force (ARTF) and the previously-mentioned ORETF. Both Task Forces have worked jointly with government regulatory agencies, including EPA. Studies that address mechanistic transfer are covered by membership in the Task Forces whereas chemical-specific studies remain the responsibility of the registrant. Specifically, the Task Forces are covering all studies except the biological monitoring test. Therefore, the following guidelines will be covered under our participation in the Task Forces:** **875.1100: Dermal exposure: Outdoor** **875.1200: Dermal exposure: Indoor** **875.1300: Inhalation exposure: Outdoor** **875.1400: Inhalation exposure: Indoor** **875.2400: Dermal exposure** **875.2500: Inhalation exposure** **875.2800: Descriptions of human activity**
25	**p. 11**	**Chart: center column, bottom row: remove $^{-1}$ from the Q_1* expression.** **Also please note that information has been submitted to revise the NOAEL currently listed as 2.0 mg/kg/day.**
26	**p. 12, ¶ 1**	**Line 2: change "only" to "do not".** **Line 7: add "on"after "based".**
27	**p. 12**	**Chart, center column, bottom row: remove $^{-1}$ from the Q_1* expression.**

No.	Location	Error
28	**p. 13, ¶ 5**	**Revise the first sentence to read: "TM was not reported to be involved in human incidents, based on the top 200 chemicals for which the National Pesticide Telecommunications Network (NPTN) received calls from 1984-1991 inclusively."**
29	**p. 14**	**Thiophanate-methyl (TM) is described as systemic, which is not entirely accurate. TM is "locally systemic" and penetrates the plant to a very small depth.**
30	**p. 14, table**	**Based on a search of the National Pesticide Information Retrieval System (NPIRS), the following changes should be made to the table: <u>Technical</u>: add 51036-310 and 66996-3 <u>Wettable powder</u>: delete IL970003. Add 1001-63, WE970003 <u>Water dispersible granules</u>: add 1001-72, 48234-7, 48234-13 <u>Granular</u>: delete 38-217 <u>Dust</u>: delete MT990008, WI970003, WI990005. Add 7501-178, ME000001, MT990004, NE000001, NJ000001, OR990059, WI990005, WI990011**
31	**p. 15, ¶ 1**	**Elf Atochem has presented information correcting the percent crop treated.**
32	**p. 15, table**	**The table inappropriately places the labeled crops into groups which do not truly share use patterns.**
33	**p. 15**	**A PHI of 50 days could not be confirmed by reading the TOPSIN M 70W label.**
34	**p. 15**	**The highest application rate for field crops is 1.4 lb ai/A (2 lb fp/A), not 1.3 lb ai/ A.**
35	**p. 15**	**The application rate for peanut seed is 0.04 lb ai/cwt and for potato seedpiece is 0.025 lb ai/cwt. The table incorrectly lists both as 0.25. However the document has used the correct application rates in risk calculations.**
36	**p. 18 et.al.**	**The use of PHED to determine the amount of exposure for an individual is appropriate but will return an unrealistic exposure if the body weight differentials are not normalized. The PHED data was meant to represent agricultural mixer/loader/applicators which are predominantly male. The average body weight for adult males is 78 kg. Therefore, the PHED data results should be normalized by body surface area for all populations which have lower average body weights.**

No.	Location	Error
37	**p. 19**	**The equation describing the calculation of the Daily Dermal Dose is somewhat vague. The final multiplier is described as the dermal absorption factor which has been defined as 7%. However, the units used insinuate that this fraction (0.07) is being multiplied by the Daily Dermal Exposure before it is used in the equation. The labeling of the term should be clarified.**
38	**p. 19**	**Assumptions section: the justification for use of female body weight is inappropriate. Using the correct body weight would reduce all adult exposures by 25%.**
39	**p. 20**	**The exposure modeling has used protection factors for personal protective equipment (PPE) which is well below accepted norms developed by either industry sources or in the open literature. Even taking the clothing penetration factors cited in OPPTS 875.1000, p. 21, where clothing penetration ranges from 6 to 50%, the penetration factor for two layers of clothing should be 25% (0.5 x 0.5), not 50%. The PHED database, used for most of the MLA exposure assessments in this document, uses more vigorous clothing protection factors (PHED analysis of all applicators with no clothing, typical clothing and PPE attached to this memo).**
40	**p. 23, ¶ 1**	**Line 4: the document indicates that "peanuts have a significant percent crop treated...". However the referenced BEAD memo lists a maximum of 4.8% crop treated. This is not a significant figure. The Gianessi documents we are providing give a figure of <1%.** **Line 10: close parenthesis does not track.**
41	**p. 23**	**The dermal penetration factor (0.07) has been omitted from the calculation of the daily dermal exposure of drill box type planting scenarios.**
42	**p. 27**	**The Agency has omitted an assessment of MLA scenarios using the WSB (water-soluble bag) formulation of the WP form. This assessment does not represent the worst case but could be useful in developing a remediation plan for the riskiest WP scenarios.**
43	**pp. 20-22**	**The Agency has used PHED to model the exposure of MLA workers. Because of overly-conservative estimates (e.g., only 50% protection factor assigned to a double layer of clothing), Elf Atochem would like to have the opportunity to use PHED to confirm the Agency's**

No.	Location	Error
44	**p. 26**	**The Agency has incorporated an exposure lifetime of 35 years for handlers of all types for TM in its LADD equation. For commercial handlers, the average employment period is less than six years. For all other users, application of TM would not occur for more than two days for each year and would certainly not occur for 35 years.**
45	**p. 29 ¶ 5**	**The Agency states that greenhouse workers may be exposed for longer periods of time due to TM's longer DFR half-life in greenhouses. The Agency has not justified this assumption vs. the predominant use of automated equipment used in commercial greenhouses of any size. If the Agency has smaller, non-automated cut-flower automation in mind, the number of exposure hours should be dramatically curtailed.**
46	**p. 30 ¶ 4**	**The Agency has used the rose and chrysanthemum DFR data supplied in the greenhouse DFR study for TM to model all greenhouse exposure. The Agency should keep in mind that mums and roses are handled much more often than most other greenhouse/hothouse varieties. The exposure assessment should be adjusted for the percentage of time a greenhouse worker is exposed to this type of flower vs. other types of horticultural products. For example, the greenhouse/hothouse exposure would vary significantly between cut and potted flowers.**
47	**p. 32, ¶ 1**	**The sentence which begins "Rain fell repeatedly during both test sites..." is very confusing and should be reworded.**
48	**p. 32**	**Under the header Study Data, the footnote 10 should be changed to 17.**
49	**p. 32**	**A statement is made that PPE is not considered viable for post-application workers even though current available literature demonstrates the importance of such equipment. This statement is inconsistent with WPS and recommendations made by the ARTF and ORETF. Specific literature articles will be provided in the near future.**
50	**p. 32**	**The rainfall alluded to in the discussion of MRID 44876301, was not of sufficient quantity at either site (max. was 0.19" on the third day after the second application in NY) to grossly affect the kinetics of dissipation. Whereas, in NY, rainfall was higher than normal for the duration of the field phase, the rainfall at that site occurred mostly towards the end of the trial when TM and MBC were already well into their respective declines.**

No.	Location	Error
51	p. 32 1st bullet bottom	Guideline OPPTS 875.2100 does not require three geographical locations. This guideline stipulates that the Agency will counsel the registrant on the number and location of measurement sites.
52	p. 32	DFR sample collection in MRID 44876301 was collected in a manner consistent which the ARTF, EPA, Canada H&W and Cal EPA recommended. Whereas the sampling techniques may deviate from OPPTS guidelines, they are still consistent with the "ARTF protocol". A full copy of this protocol will be appended.
53	p. 32	Per the recommendations of the EPA to all ARTF members, Elf Atochem staff discussed all DFR studies with EPA representatives prior to execution. The number of sites used in the apple DFR study was pared from three to two during discussions with EPA representatives.
54	p. 32 2nd bullet	The 10 gal/ A dilution rate is used only for aerial applications. As the study was conducted with airblast sprayers, the dilution rate was dependent on the proper methodology for this application technique. The 100 gal/ A rate used approximates the lowest such rate that provides adequate coverage of the trees and is consistent with commercial practice.
55	p. 32, ¶6 to p. 33, ¶1	The document lists seven items for MRID 44876301 as deficiencies from current guidelines. Of these seven items, only the second item is a departure from the guidance. Items 1, 3, 4, 6 and 7 are either departures from the study protocol or are allowed by EPA instructions to ARTF members. Item 5 is in error and contradicts the facts stated in the study report.
56	p. 33 ¶ 3	The calculations of the half-lives cited in the text (3.8 and 31 days) have not taken into account the biphasic modality of normal decline in nature. This effect renders these results incorrect and is the major reason for the abruptly lower regression coefficient for the WA data. The NY analysis is not harmed as greatly by this defect as a the time interval covered by the overly-simplified pseudo-first-order model was limited to only 21 days whereas the entire 81-day data set was included in the calculation for the WA half-life.

No.	Location	Error
57	**p. 34**	**The document lists four items for MRID 44866201 as deficiencies from current guidelines. None of the items in this list depart from current guidelines for this type of study. Items 1 and 4 relate to the specifics of the protocol and were executed in accordance to instructions from EPA to either the ARTF or to Elf Atochem. Item 2 is an omission from the report which is not required per the guidelines but can be recouped from the raw data. Item 3 is not a guideline issue and does not contain sufficient information for adequate assessment.**
58	**p. 34, ¶ 5**	**The document states that the application of 3336WP was performed at rates "up to 2.5 times the cited rate" but does not offer an explanation for this observation. The report is consistent with the application of 8 oz fp/ A two times with a 7-day interval.**
59	**p. 35 ¶ 1**	**The document states that TM residues peaked at the 8-12 hour interval after the second application in GA and PA, but this is also true for the CA site.**
60	**p. 35**	**The half-lives calculated by the Agency vary significantly from our calculations but, without more detail, we cannot offer input. A statement made earlier on the page insinuated that the Agency did not agree with our biphasic approach because of failure to explain the fact that TTRs maximize after application. There are many possible explanations for this effect but such explanations were not included as they were speculative and not a requirement per any EPA guidance for TTR studies. The most likely cause for this effect is that, when measuring DFR (not exhaustive residues), other ingredients included in formulations may inhibit the short-term availability of the active ingredient to dislodging with detergent water or a cotton sheet.**
61	**p. 35, ¶ 2, line 11**	**Initial deposition TTR should be labeled as percent of deposition.**
62	**p. 36**	**There is insufficient data included from the 1997 literature study by D. H. Brouwer, et al., for effective comment. However, kinetics of decline are usually not dramatically affected by a mere 2X difference in C_0. This finding is inconsistent with physico-chemical theory.**

No.	Location	Error
63	**p. 36**	**There is insufficient data included from the 1992 literature study by D. H. Brouwer, et al., for effective comment. However, the conclusion that there is no significant decline in DFRs over 60 days is inconsistent with both our study and Brouwer's own 1997 study. Irrigation alone would have forced a decline in the DFRs, even if photoloysis was somehow negated.**
64	**p. 37 ¶ 1**	**The Agency states that the referenced Brouwer publications's reported TM half-life of between 22 and 41 days supports Elf Atochem's conclusions from the submitted greenhouse DFR. Our DFR study determined the half-lives to be 18.2 and 18.9 for roses and mums, respectively. These half-lives are not the same as those in the Brouwer publication.**
65	**p. 38 ¶ 2**	**Application to 100% of the crop is incorrectly assumed. More realistic data are being provided.**
66	**p. 38-39**	**The post-application cancer risk calculation presumes an exposure life of 35 years. Later, the Agency admits that average commercial exposure is 5.35 years. The Agency may be erroneously adding yet another 10x factor to the risk assessment by adhering to this improbable scenario.**
67	**p. 39**	**The REIs calculated for apples are inordinately high due to miscalculation of the half-lives, as noted in an earlier comment on the contents of page 33.**
68	**p. 39 ¶ 2**	**Although we have no data concerning the work pattern for greenhouse workers, we question the Agency's use of 120 days for cut-flower harvesting, which seems excessive. Cut-flower horticulture comprises only a fraction of greenhouse/hothouse activity. In the U.S., the cut flower market accounts for only 5% of total horticultural sales.**
69	**p. 39, ¶ 2, line 9**	**Typographical error: the exponent has been left off one of the "10"s.**
70	**p. 40 last ¶**	**The 300 lb fp/ A/ season scenario is only used for drench treatments and does not reflect other use patterns. Further information will be provided.**
71	**p. 42**	**Per PLCAA (Professional Lawn Care Association of America) data, the average lawn is 0.17 acre, much less than the 0.5 acres used as a default.**

No.	Location	Error
72	**p. 42**	**"Belly-grinders" are not used to spread granular formulations over entire lawns. These applicators are used mostly on flower beds or ground cover.**
73	**p. 43**	**The formulation is usually applied once per season, if that, by residents. The application frequency of five applications per season is not borne out by market data. Even in the worst case where TM is included in a fertilizer product, the manufacturer (Scotts) recommends this combination be applied only once per year.**
74	**p. 44**	**For the homeowner use scenario, an assumption was made "on treatment of ½ acre lawn per day,..". TM is not used every day by homeowners.**
75	**p. 44**	**Per PLCAA data, the average lawn is 0.17 acre.**
76	**p. 44**	**The LADD equation presumes yearly application of TM on a resident's lawn and a use life span of 35 years. Both of these presumptions are not borne out by market data.**
77	**p. 45**	**Belly grinder application is not used to apply any TM product over a lawn.**
78	**p. 46**	**The RED acknowledges that one application per season is normal practice, but assumes 5 on page 44, then says 6 or more applications per season are common on page 57. Applying top label rate to ½ acre of turf 5 times per season would cost several hundred dollars. This is not average use.**
79	**p. 47**	**The Agency has postulated mowing activity of 1-2 hours over an average lawn of 0.5 acre. This can only be achieved via a mowing tractor, which should render a Tc which approaches zero, effectively negating risk.**
80	**p. 48**	**The TC for adults involved in heavy yardwork (14,500 cm^2/hr) is 50% greater than the highest agricultural reentry Tc. This value is comparable to field workers who immerse themselves in tall crops such as corn. Whereas a homeowner may crawl on turf to weed, aerate or dig, the contact area is limited to the lower legs, forearms and hands.**
81	**p. 49**	**The formula for PDR for granule ingestion by toddlers lacks a factor for the attenuation of TM content due to watering in of the treatment per label directions. Moreover, the application of granular material results in an average of 1 granule/ sq. in.. Ingestion of 0.3 g of this very light formulation would require a very dextrous and dedicated toddler ranging over a considerable area of property. Moreover, only the corncob-based granular formulations should be used for this calculation as toddlers would find fertilizer-based granules unpalatable.**

No.	Location	Error
82	**pp. 50-51**	**The equation for incidental soil ingestion presumes that 100% of the TM applied to turf is in the soil right after application of the WP formulation. This assumption is not true.**
83	**p. 51**	**Foliar contact DFR values would also be well below the limit of quantitation of our DFR methodology.**
84	**p. 51**	**Main paragraph: the EPA has taken the liberty of assuming reentry will occur even though the label prohibits it. Elf Atochem believes this assumption is inappropriate.**
85	**p. 55**	**The table should indicate in the header what the numbers within it represent.**
86	**p. 55**	**The table lists an MOE for toddlers harvesting fruit.**
87	**p. 55**	**The wrong NOAEL (2 mg/kg) was used to calculate the MOEs for non-occupational exposures. Elsewhere in this document Elf Atochem has presented the information necessary for reconsideration of the NOAEL. The MOE will increase by 7 to 50 fold depending on which of the two NOAELs identified for non-occupational exposure is used.**
88	**p. 55 ¶ 3**	**The assessments for adults harvesting fruit from home orchards is based on the use of TOPSIN M WP, which is not sold for residential use. Moreover, these home orchards are not of adequate size or quality to require forty minutes of harvesting per day.**
89	**p. 57**	**The document presumes five applications of TM per year to golf courses.**
90	**p. 58**	**The document contains an assertion that the instructions to water the products in does not prevent contact with turf prior to watering in. Whereas this is true, the chronic exposure proposed for this opportunistic scenario should not be equal to the time of exposure allotted to proper use of the product.**
91	**pp. 63-68**	**The protection factor accorded to each layer of clothing (50%) is overly conservative in comparison with ARTF/ ORETF, PHED and literature values. An example PHED analysis is attached as an example.**
92	**p. 63**	**Neither the dry flowable nor the water-dispersible granules are used for field crop application.**
93	**p. 63-69**	**The potato seedpiece treatment scenario is not addressed in Table 4.**
95	**p. 68**	**Belly grinders are not used to apply granular formulations over large areas of turf (1 acre is the default listed).**

No.	Location	Error
96	**p. 68**	**The agency has earlier stated that the average lawn is 0.5 acre while PLCAA asserts it is only 0.17 acre. The default of 2-3 acres is not reasonable. Moreover, this large an area would not be treated with a push spreader by one individual.**
97	**p. 70**	**The Agency has use the results of an earlier captan study to extrapolate an inhalation exposure for potato planters that has an MOE of only 61. The original captan study quantified inhalation exposure for a worker with no inhalation protection. The Gustafson labels for the potato seedpiece dust products require the use of a NIOSH-approved respirator, thereby negating inhalation exposure.**
98	**p. 70, table**	**The inhalation MOE is not representative of the Gustafson label. The captan study on which these assessments are based measured inhalation exposure using gauze pads fitted into a gas mask, thereby simulating unprotected workers. Both Gustafson potato seed piece dusts containing TM require the used of MSHA/NIOSH-approved respirators which would cut the exposure to insignificant amounts. As the inhalation MOE is the only MOE less than 100, this factor would remove the practice of filling the hopper as a concern. Additionally, the Gustafson label requires more PPE than was used in the captan study for dermal exposure.**
99	**pp. 71-90**	**The potato seedpiece treatment scenario is not mentioned in any of the tables that stipulate the inputs and results of the risk assessment for various occupational scenarios.**
100	**p. 71**	**The highest application rate amenable to airblast application is 2 lb fp/ A or 1.4 lb ai/ A.**
101	**p. 71**	**Only the 70% WSB formulation is used in airblast applications.**
102	**p. 74**	**Only the 70% WSB formulation is used in airblast applications.**
103	**p. 76**	**Belly grinders are not used to apply granular formulations over large areas of turf.**
104	**p. 77**	**Table 8 supposedly lists the risk assessments for applicators using additional PPE (coveralls) over the scenarios in Table 7. The MOEs in Table 8 are lower than those in Table 7. The opposite situation should exist.**
105	**p. 82**	**Only the 70% WSB formulation is used in airblast applications.**
106	**p. 86**	**The highest application rate in agriculture is 2.25 lb fp/ A or 1.73 lb ai/ A.**
107	**p. 86**	**Only the 70% WSB formulation is used in airblast applications.**

No.	Location	Error
108	**p. 87**	**Only the 70% WSB formulation is used in airblast applications.**
109	**p. 87**	**The highest application rate in agriculture is 2.25 lb fp/ A or 1.73 lb ai/ A.**
110	**p. 88**	**Only the 70% WSB formulation is used in airblast applications.**
111	**p. 88**	**The highest application rate in agriculture is 2.25 lb fp/ A or 1.73 lb ai/ A.**
112	**p. 88-89**	**The application rates for scenario 9 are too high. Per Cleary data, the typical application rate is about 5 lb ai/ A. The maximum turf application rate is 10.9 lb ai/ A which is used as the typical application rate.**
113	**p. 89**	**The first column, headed Application Rate, includes some risk assessment numbers which should not be there.**
114	**p. 90**	**Belly grinders are not used to apply granular formulations over large areas of turf.**
115	**p. 91**	**A hand-planting Tc of 10,000 for all crops is not borne out by the ARTF model.**
116	**p. 91**	**For field crops with low contact, the EPA used a Tc = 2,500 for harvesting celery. However, the ARTF Tc for celery is 946.**
117	**p. 91**	**For field crops with medium contact, EPA used Tc = 4,000 for scouting, irrigating, hoe and hand harvesting. However, the ARTF Tc for such examples as cucurbits and strawberries is 946.**
118	**p. 91**	**For field crops with very high contact, EPA used a Tc = 10,000. However, the ARTF value for such examples as the harvesting snap beans was only 528.**
119	**p. 91**	**For turf activities, EPA used a Tc = 10,000 for cutting, rolling and harvesting sod. However, the ARTF determined a Tc of 946 for these activities.**
120	**p. 91**	**For tree crops (including ornamentals), EPA used a Tc of 10,000 for all activities requiring contact with foliage in crops such as stone fruits and nuts. The ARTF has determined a Tc of 92 for almond shaking and apple pruning. The ARTF Tc for apple harvest and thinning is 2431.**
121	**p. 91**	**EPA proposes a Tc of 4,500 for greenhouse. However, ARTF has developed a Tc of 654 for nursery harvest and a TC of 88 for nursery pruning.**

No.	Location	Error
122	**p. 93**	**The half-lives listed in Table 16 were calculated using a flawed model that does not recognize the natural compartments that exist in environmental decay. This defect results in overly-long half-lives and, therefore, lower r^2 numbers, lower slope values and lower C_0 values.**
123	**p. 93**	**As stated earlier, most of these half-lives are too long due to systematic bias in the calculation. The chemical's two-compartment decline mode was not factored into these calculations. By using a simple uniphasic log-linear decay assumption that underestimates exposures for the first few days and overestimates exposures for the remaining time, the EPA has inflated the REI by two-fold and more.**
124	**pp. 94-10**	**Because these assessments are based on a faulty predictor of DFR values, the risk assessments are unrealistically high.**
125	**pp. 105-109**	**These values are based on the high application rate of 8 oz fp/1,000 sq. ft. (fp = 50% ai) although the text claims it's typical. The typical rate is 2-4 oz fp/ 1,000 sq. ft.. Moreover, these data are also based on a faulty model that does not incorporate the compartmentalized nature of pseudo-first-order decay.**
126	**pp. 110-111**	**These assessments were based on faulty modeling of the cut-flower DFR study and an unrealistically high Tc. Value.**
127	**p. 112**	**Belly grinders are not used to cover large areas of turf.**
129	**p. 115 – 116**	**These values are based on the high application rate of 8 oz fp/ A (fp = 50% ai) although the text claims it's typical. The typical rate is 2-4 oz fp/ A. Moreover, these data are also based on a faulty model that does not incorporate the compartmentalized nature of pseudo-first-order decay.**
130	**pp. 117 – 118**	**These values are based on the high application rate of 8 oz fp/ A (fp = 50% ai) although the text claims it is typical. The typical rate is 2-4 oz fp/ A. Moreover, these data are also based on a faulty model that does not incorporate the compartmentalized nature of pseudo-first-order decay. The Tc used was also too high when compared with the findings of the ARTF.**
131	**p. 119**	**In addition to over-conservative bias, this table uses the agricultural scenario for homeowner orchards. Homeowners apply TM before fruit-set, which would negate any appreciable DFRs of either TM or MBC on the foliage or fruit by fruit maturity.**
133	**pp. 121-123**	**The scenarios for non-dietary TM ingestion by a toddler are also overly-conservative.**

ERROR COMMENTS
SECTION H
Occupational and Residential Exposure Assessment and Recommendations for the Risk Assessment Document for Carbendazim (MBC), dated June 21, 2000, DP Barcode D265419

Note: Elf Atochem cannot take full responsibility for the review of this section, since it concerns registrations and uses with which we are not involved.

No.	Location	Error
1	p. 9	Table header incorrectly lists 'Thiophanate-methyl' rather than MBC.
2	p.11, ¶1	The Agency has omitted a CMA study on exposure but not included enough detail in the document for assessment of that rejection.
3	p. 11, ¶1	The Agency has used a baseline assumption that addition of MBC to paints is similar to mixing/loading of wettable powders. For that reason, PHED was used to model exposure. However, the Agency has not included sufficient justification for this assumption. A reasonable assumption that a factory scenario (indoor, climate-control, low humidity) would greatly mitigate exposure factors cannot be dismissed due to this lack of justification.
4	p.12, ¶1	The Agency is equating 13-year-olds with adults which will lead to errant conclusions later on in this assessment.
5	p.12, ¶2	The Agency used PHED to estimate exposure to handlers of all types with the worst-case being defined as females 13+ years of age. However, PHED data were collected almost exclusively on adult males of about 80 kg bw. As the Agency is basing their calculations on the mg ai/ lb ai handled, this assumption will lead to greatly exaggerated exposures due to the larger body area afforded by the adult males on which the PHED was based. A correction factor for body area between adult males and females 13+ years of age should be included in this assessment.
6	p. 12, ¶ 4	The Agency has assumed what seems to be extraordinary efficiency for professional painters but has not stated whether or not market data was used as a basis.

No.	Location	Error
7	**p. 13, ¶ 4**	**The Agency has allowed only a 50% protection factor for a double-layer of clothing. This factor is much too low. In the EPA's own guidance, the lowest protection factor cited for a single layer of clothing is 50%. Therefore, a double layer of clothing should be given at least a 75% protection factor. The PHED itself attributes a much greater protection factor for each layer of clothing.**
8	**p. 13, ¶ 7**	**The Agency has not justified its assumptions for an individual adding MBC during paint manufacture as a discussion of whether or not this procedure is automated is lacking in this assessment. An individual exposed to MBC either from the manufacture of paints or painting probably will not do so for 35 years. Moreover, private homeowners do not paint every year for 50 years.**
9	**p.15, ¶ 7**	**The Agency should survey paint manufacturers to determine whether or not the addition of MBC to paint is automated or the median occupational duration for a line employee mixing any one ingredient into paint as 35 years is an unrealistic assumption. If there is a mix of scenarios, the Agency should include only the fraction of human mixers in their occupation assessment much like they do with ag market data.**
10	**p. 16, ¶ 2**	**The Agency is accepting the use of PPE in domestic settings for painting but does not allow it as an option for agricultural chemicals.**
11	**p. 16**	**The Agency's use of a 13-year-old female as a possible participant in most of the scenarios listed on this page is unrealistic.**
12	**p. 19, ¶ 2**	**The Agency is presuming that MBC is readily available for intake by residents sprinkled with MBC paint. The low vapor pressure of MBC plus its sequestration in the paint upon drying make this assumption highly doubtful.**

ERROR COMMENTS
SECTION I
THIOPHANATE METHYL - Report of the FQPA Safety Factor Committee, dated July 1, 1999, HED Doc. No. 013546

No.	Location	Error
1	**p. 2, ¶ 3**	**The FQPA Committee indicated that: "Evidence of increased susceptibility was seen following *in-utero* exposure to rabbits wherein developmental toxicity (increased fetal/litter incidence of asymmetrical pelvis and possibly other rib and vertebral variations) was observed at a dose which was lower than that causing maternal toxicity" (line 1)** **We disagree with the Agency assessment of increased sensitivity of the offspring because:** • **A weight of evidence approach was not taken by the Agency. Results from the repeat rabbit developmental toxicity study (Argus 1997 - MRID No. 45051001) were not considered by the Agency. No evidence of increased susceptibility was noted in the repeat study, in which the developmental toxicity NOAEL is greater that the maternal toxicity NOAEL.** • **In the first study (LSR 1986 - MRID 40022801), the developmental toxicity NOAEL should be 20 mg/kg/d and not 2 mg/kg/d as erroneously established by the Agency. The fetal and litter incidence of asymmetric pelvis were not significantly increased at any of the doses tested(2, 6 and 20 mg/kg/d). All other skeletal variations noted in this study were also not statistically significant from controls and were of "uncertain toxicological significance" as indicated by the EPA reviewer.**

2	**p. 2, ¶ 3**	**The FQPA Committee indicated that: "No evidence of increased susceptibility was demonstrated following pre and/or postnatal exposure to thiophanate-methyl for two generations; effects in the offspring occurred at the same dose that caused parental toxicity." (line 8)** **The Agency's conclusion that the effects in the offspring occurred at the same dose that caused parental toxicity contradicts the Revised Toxicology Chapter (Table 2 on page 12 and Reproductive toxicity on pages 15 and 16) The offspring NOAEL and LOAEL were established at 13.7 mg/kg/d and 43.3 mg/kg/d, respectively whereas the parental NOAEL and LOAEL were, respectively, < 13.7 and 13.7 mg/kg/d.**
3	**p. 3, ¶ 1**	**As stated elsewhere, thiophanate-methyl is not a systemic fungicide. It is only locally systemic.**
4	**p. 3, ¶ 2, line 1**	**It appears that the reference to "benomyl" on this line should in fact read "thiophanate-methyl."**
5	**p. 4, ¶ 5**	**Rationale for Requiring the FQPA Safety Factor** **The FQPA rationale was based on:** **a) There is evidence of increased susceptibility of developmental toxicity studies in rabbits** **b) There are data gaps for acute and subchronic neurotoxicity studies in rats, and** **c) A developmental neurotoxicity study in rats is required** **We disagree with the Agency's rationale of "increased susceptibility" based on the aforementioned information and believe that a FQPA safety factor of 3 would be more appropriate in the absence of neurotoxicity data.**

ERROR COMMENTS
SECTION J
Thiophanate-methyl: HED Preliminary Risk Assessment for the Reregistration Eligibility Decision (RED) Document, dated June 22, 2000, DP Barcode D230340

No.	Location	Error
1	General	Since this document contains information drawn from all the Chapters, when errors are corrected elsewhere they should be corrected here. Due to the level of detail, Elf Atochem may not have been able to correct each incidence of error in this summary document.
2	p. 5, ¶ 2, line 3	TM is manufactured by Nippon Soda Company Ltd. of Japan, not by Elf Atochem. NISSO TM LLC and Gowan Pacific LLC are the technical registrants. The TOPSIN M trade name is owned by Nippon Soda Ltd.
3	p. 5; ¶ 4; line 14	Independent method validation was completed and has been submitted to EPA (MRIDs 44526101, 44703602))
4	p. 5, line12	The correct number of registrations is 36 active and 22 Special Local Need. The range of ai for TM formulations should be 1.65% to 90%
5	p. 5, line13,14	Major food/feed crops include: (should say) dry beans, sugarbeets, wheat, apples, green beans, and potatoes (seed pieces).

No.	Location	Error
6	**p. 6, ¶ 2**	**The Agency indicated that "Thiophanate-methyl is generally more toxic than MBC for adverse developmental effects".** **We disagree with the Agency statement and request the Agency's clarification in light of:** • **Developmental toxic effects with Thiophanate-methyl occurred in rabbits and were absent in rats. MBC produced developmental toxic effects in both species with more significant findings in rats** • **The skeletal anomalies associated with Thiophanate-methyl were neither biologically nor statistically different from concurrent controls. Those noted with MBC were both statistically and biologically different from controls. In rats, MBC produced exencephaly, domed head, anophthalmia, microphthalmia, bulged eyes, etc.** • **If "more toxic" was based on the number of the developmental findings (page 6, 3rd paragraph) then the comparison was completely inaccurate (see below).** • **If "more toxic" was based on a comparison of the developmental toxicity NOAEL, then it should be noted that the developmental toxicity established for Thiophanate-methyl at 2 mg/kg/d in rabbits was incorrect and refutable.** • **Thiophanate-methyl did not produce reproductive adverse effects whereas MBC was associated with reduced sperm count, reduced testicular size and testicular pathology.**
7	**p. 6, ¶ 3**	**The reviewer stated that "Fetal effects from Thiophanate-methyl exposure include ocular malformations, increased mortality, reduced fetal weight, brain malformations, cleft palate and delayed skeletal and visceral maturation"** **We disagree with the reviewer in light of:** • **Ocular malformations, brain malformations, cleft palate and visceral maturation were not associated with Thiophanate-methyl. Delayed skeletal ossification and skeletal variations were the only findings noted with Thiophanate-methyl in rabbits. This is substantiated by the reviewer's own conclusion under the Developmental/Reproductive Toxicity section on page 17.**

No.	Location	Error
8	**p. 7, ¶ 2**	**We disagree with the Agency selection of the developmental toxicity NOAEL of 2 mg/kg/day from the rabbit study in the risk estimates in light of:** • **The fetal and litter incidence of asymmetric pelvis were not significantly increased at any of the doses tested(2, 6 and 20 mg/kg/d) in the referenced study (LSR 1986 - MRID 40022801).** • **All other skeletal variations noted in this study were also not statistically significant from controls and were of "uncertain toxicological significance" as indicated by the EPA reviewer.** • **The findings of asymmetric pelvis were of uncertain toxicological significance and were not detrimental to the fetuses as evidenced by the lack of effects on fetal weight and litter size.** • **A weight of evidence approach was not taken by the Agency when evaluating the developmental toxicity potential of Thiophanate-methyl in rabbits. Data from a second developmental toxicity in rabbits (Argus, 1997 - MRID No. 45051001) that was submitted to the Agency were not included in the HIARC evaluation. No developmental toxic effects were noted in this repeat study.** • **The developmental toxicity NOAEL should be 20 mg/kg/d and not 2 mg/kg/d as erroneously established by the Agency.**
9	**p. 7, ¶ 3**	**The Agency recommended a dermal absorption rate of 7%. While we previously agreed with the Agency's determination, a dermal absorption study using human skin revealed a rate of 0.07% for the neat material (An-Ex Analytical Services, Report No. RPUK/2/93/R2 dated 09/17/93. Study to be submitted)**
10	**p. 8; Dietary Exposure & Risk; pp2**	**Line 5: The lifetime cancer risk is a lifetime aggregate dietary cancer risk that includes MBC from benomyl. The lifetime cancer risk is listed as 1.6E-7 for thiophanate-methyl. This should read 1.6E-6.**

No.	Location	Error
11	**page 9; pp1; line 4**	**Both aggregate assessments, TM and MBC (TM use) and TM and MBC (all uses) both yield a total thiophanate methyl and MBC dietary cancer risk of 2 E-6 (see Page 80; pp1; line 2). Based on page 82, Table 20, it would appear that 2 E-6 is an aggregate risk for TM and MBC (all uses).**
12	**Page 9; Water Exposure and Risk; pp1; line 1**	**Monitoring data from USDA Pesticide Data Program (PDP) is available for MBC residues for certain food commodities. This data should be used for developing a more accurate risk assessment of MBC residue dietary exposure. It is also possible to approximate thiophanate-methyl residues at the consumer level by using the average ratio of TM to MBC within residue studies and applying the ratio factor to the PDP data. Because thiophanate-methyl residues dissipate more rapidly than MBC residues, such an assessment would still be very conservative.**
13	**p. 9; Water Exposure and Risk; pp3; line 10-14**	**In the environment, thiophanate-methyl may also degrade by routes that do not require intermediate formation of MBC. Formation of MBC from thiophanate-methyl requires an intramolecular reaction that creates the benzimidazole ring, common to MBC. Thiophanate methyl has carbamate and thiocarbamate linkages that may be cleaved by nucleophilic attack, providing opportunity for further degradation through routes alternative to MBC. For example, strawberry and turf DFR studies demonstrate rapid degradation of thiophanate-methyl; however, very little MBC is formed. As MBC is not prone to photolytic degradation or any other rapid degradation processes, it is reasonable to conclude that the majority of parent compound does not degrade through the MBC pathway. As such, any assessment of surface water contamination by MBC based on the degradation of thiophanate-methyl should take into account the fact that photolytic degradation yields little MBC. The EPA's assessment of MBC drinking water risk for surface water from thiophanate-methyl application does not take into account this phenomenon.**
14	**p. 9; Water Exposure and Risk; ¶ 4**	**Next to last line: "not: should be "nor"**

No.	Location	Error
15	**p. 10; ¶3; line 1**	**Worker risk calculations utilized DFR data generated by Elf Atochem. However, the half-lives derived by the EPA are in error. The half-life of thiophanate-methyl, as determined by EPA using a nonlinear regression analysis for an apple dislodgeable foliar residue (DFR) dissipation study conducted in Washington, was reported to be 31.4 days. However, the decline curve was carefully evaluated by Elf Atochem and determined to be biphasic. The decline of TM between the second application and 28 days after the second application yielded a half-life of 17 days. This value is also comparable to the residue decline of 12 days calculated between the first and second application. The correlation coefficient associated with the residue decline after the second (last application) is very good ($r^{2=}$ 0.9372 for an r=0.9681) whereas the correlation coefficient for the decline curve when extended to include all data points up to the final sampling at 84 days is poor.**
16	**p. 12; ¶ 2; line 5**	**We disagree with the sentences, "Because the PDP analytical method quantifies total MBC residues from all sources (both benomyl and thiophanate-methyl), it is possible that the aggregate dietary exposure and risk estimates (from benomyl and thiophanate-methyl) may be overestimated to an unknown degree. However, this overestimation is expected to be negligible relative to the use of field trial data used to estimate(ed) MBC exposures from thiophanate-methyl use." There is a clear overestimation of MBC risk by utilizing PDP data for determination of benomyl related MBC residues and aggregating that data with MBC field trial data for thiophanate-methyl residues. This is a disparate approach that could be easily harmonized by using the PDP data for assessing MBC residues from thiophanate-methyl which is reflected in the PDP data set. Further, if required, separating the relative risk from benomyl and benomyl derived MBC from thiophanate-methyl derived MBC could be accomplished by comparing residue data between the two compounds. It should be noted that there is no logical rationale for using PDP data for calculating MBC residues derived from benomyl but not for MBC residues derived from thiophanate-methyl. The development of PDP derived thiophanate methyl residue data could also be accomplished by comparing thiophanate methyl and MBC residue levels in residue studies.**

No.	Location	Error
17	**p. 12; pp4; line 2**	**This statement is premature given the fact that the risk assessments have not yet been refined. MBC residues in groundwater are very low and TM is expected to pose no risk. Also, the risk to surface water is greatly overstated based on the current assumptions being used.**
18	**P. 14, ¶ 2, line 1**	**TM ai % is incorrect and should be changed to 97%. The correct number of registrations is 36 active and 22 Special Local Need.**
19	**p. 17**	**Carcinogenicity. The Agency indicated that "In males, a positive increasing trend and pair wise increase in the incidence of adenomas, carcinomas and combined adenomas/carcinomas at the HDT were observed." We disagree with the Agency since no carcinomas were noted in male rats (see page 9 of the Revised Toxicology Chapter). It is unclear why a pair-wise analysis was conducted for combined adenomas/carcinomas in males. It should be indicated that the HDT (6000 ppm) was considered excessive and the MTD was exceeded based on excessive mortality noted in males (see page 9 of the Revised Toxicology Chapter).**
20	**p. 29, ¶2**	**TM is manufactured by Nippon Soda Company Ltd. of Japan, not by Elf Atochem. NISSO TM LLC and Gowan Pacific LLC are technical registrants. The TOPSIN® M trade name is owned by Nippon Soda Company, Ltd. Line 2: TM is not registered for forestry uses.**
21	**p. 29, ¶ 3, line 5**	**Elf Atochem has not advised the Agency that it does not intend to support bananas.**

No.	Location	Error
22	**p. 29, ¶4**	**BEAD estimate of annual usage for ag crops is low. Elf Atochem sales are closer to 400,000 lbs ai. vs BEAD estimate of 300,000 lbs ai. The largest TM markets are dry beans (27%), sugar beets (14%), wheat (13%), potatoes (23%), apples (17%). Most of the usage is in CA, ID, ND, MN PA, VA, FL. Next sentence doesn't make sense ...."Crops with a high percentage of their total US planted acres treated include..(crops listed do not have a high percent of their acres treated) plums (1%), almonds (9%), pecans (4%), and green beans (6%).Celery use has been canceled Error in list of crops with less than 1% treated acres. - should be celery, cherries, peanuts, onions, soybeans, wheat (Gianessi, National Center for Food and Agricultural Policy (NCFAP) 1997).**
23	**p. 30; pp3; line 2**	**Animal storage stability data has been submitted to EPA (MRIDs 44643502, 44592301)**
24	**p. 30; Plant Metabo-lism; pp1**	**EPA should be consistent with its procedure for determining 2-AB residues, either the TM or MBC ratio can be used, however, not both. MBC is closer to 2-AB on the metabolic route than is TM to 2-AB. For this reason, using the residue level of only MBC to calculate 2-AB residues would be a more appropriate relationship. Also, unlike TM, both compounds are benzimidazoles.** **Elf Atochem also believes that it is incorrect to include residue levels of 2-AB that were extracted through acidic reflux conditions. The bound residues are not soluble and would not be bioavailable when ingested.**
25	**Pg. 31; Residue Analytical Methods-Plants and Animals; pp3**	**Line 19: Independent method validation was completed and has been submitted to EPA (MRID 44703602)**

No.	Location	Error
26	**Pg. 32; Methods for determin-ation of residues in/on animal commo-dities**	**Line 2: Elf Atochem has provided EPA with a proposed enforcement method and has provided an independent laboratory validation study (MRID 44526101).**
27	**Page 32; Storage Stability; pp1; line 3**	**No storage stability studies on MBC are required. On June 18, 1996, EPA met with Elf Atochem to determine what storage stability data would be required to support studies being submitted at that time. At the meeting, the Agency stated that submitted storage stability studies demonstrated that MBC was highly stable when stored frozen and that this data could be extrapolated up to 5 years demonstrating satisfactory stability of MBC. On this basis, the EPA stated that no additional residue data was required for MBC. Interim reports for thiophanate-methyl have been submitted to the EPA on a 6 month basis for the past several years, in accordance with the Agency's decision that only storage stability data would be required for the parent compound.**
28	**p. 32; Storage Stab.; ¶ 2**	**see previous comment**
29	**Page 32; Storage Stab.; ¶ 3**	**Elf Atochem has submitted storage stability data for thiophanate-methyl and MBC in animal commodities that demonstrates stability to support all samples analyzed for milk and tissues. This data was included as a separate submission (MRID 44592301, 44643502).**
30	**Page 33; ¶ 3; line 1**	**Residue studies have been submitted to the EPA for the following commodities: dried peas, watermelon, squash, cucumbers, peanuts, pecans, potatoes, soybeans, sugar beets.**
31	**Pg 33; ¶ 4; line 1**	**If, as stated above, the reregistration requirements are fulfilled for apples and plums, no further data should be required.**

No.	Location	Error
32	**Pg 33; Pending Petitions;¶ 2**	**Line 6: Additional grape trials have been completed and will be submitted.**
33	**Pg 33, Mag. of residue in processed Food/Feed**	**Line 5: Processing studies have been submitted to the EPA for the following commodities: peanut (44850901), potato (44498502), soybean (44572702), and sugarbeet (44584601).**
34	**Page 35; pp2; line 3**	**The combined residues of MBC in whole milk was 0.034 ppm TM equivalents and for skim milk 0.044 ppm. Tolerance should be established as 0.1 ppm, not 0.15 ppm. The combined residues of TM and MBC in muscle, fat, and liver was <0.045 ppm TM equivalents and <0.075 ppm in kidneys. Tolerance should be established at 0.1 ppm, not 0.15 ppm.**
35	**p. 36; Field Accum. in Rotational Crops; ¶ 1**	**Line 2: Field crop rotational studies have been conducted with TM. These studies will be submitted to EPA in October, 2000.**
36	**Page 37;¶ 2; line 5**	**Residue Chemistry studies for almonds (44487001), pecans (44498501), and peanuts (44515701) have been submitted to EPA.**
37	**Page 37; ¶ 2; line 5**	**Monitoring data from USDA Pesticide Data Program (PDP) is available for MBC residues for certain food commodities. This data should be used for developing a more accurate risk assessment of MBC residue dietary exposure. It is also possible to approximate thiophanate-methyl residues at the consumer level by using the average ratio of TM to MBC within residue studies and applying the ratio factor to the PDP data. Because thiophanate-methyl residues dissipate more rapidly than MBC residues, such an assessment would still be very conservative.**
38	**p. 37, ¶ 3**	**Our data (Gianessi 1997) shows cherries less than 1%, apricots 3%, nectarines1%, peaches 5%, and melons (cantaloupes 2%, melons 1%). Sugar beets (9%), onions less than 1%, cucumbers 1%, squash 1% vs. EPA that shows these last crops at 100% CT. See confidential attachment for potato information.**

No.	Location	Error
39	**Page 37; pp5; line 4**	**Processing studies have been submitted to the EPA for the following commodities: peanuts, potatoes, soybeans, sugar beets.**
40	**Page 40; pp2; line 2**	**The TM cancer risk estimate is listed as 1.6E-6 in this section and 1.2E-7 according to Table 20 of this document. The MBC cancer risk estimate is listed as 4.3E-7 in this section and 4.7E-7 according to Table 20 of this document.**
41	**Page 40; ¶3; line 3**	**Both aggregate assessments, TM and MBC (TM use) and TM and MBC (all uses) both yield a total thiophanate methyl and MBC dietary cancer risk of 2 E-6 (see Page 80; pp1; line 2). Based on page 82, Table 20, it would appear that 2 E-6 is an aggregate risk for TM and MBC (all uses).**
42	**Page 41; (c)**	**Elf Atochem agrees with the EPA's statement and suggests that the EPA consider using the 95th or 99th percentile residue for thiophanate-methyl, recognizing that the compound is short lived in the environment and that MBC is more persistent. This approach should at least be used for the aggregate risk assessment that includes both parent and MBC residues. This decision is especially supportive for an acute risk assessment where it is inconceivable that 99th percentile residue for both compounds could yield a realistic acute based risk.**
43	**Page 41; (d)**	**Elf Atochem has completed a consumer washing study for evaluating the extent of thiophanate-methyl reduction due to washing. This study will be submitted in the near future.**
44	**Page 42; Table 6**	**Due to discrepancies with Table 20 in this document, it is not clear whether the MBC exposure includes the MBC from benomyl component.**

No.	Location	Error
45	**Page 44; Estimated Environ-mental Concen-trations; ¶ 1; line 4**	**Modeling was used to estimate surface water concentrations from use of TM at maximum application rates and frequencies. The EPA assessment is based on a worst case assessment using a Koc of 117.7. Use of this Koc is highly conservative and represents a worst case evaluation. Thiophanate methyl Kocs have been determined to range from 117.7 - 858.8 for a variety of soils. Elf Atochem intends to provide the EPA with a more refined modeling assessment. Calculations of MBC residues in surface water based on the factor of 82.7% conversion of thiophanate-methyl to MBC are exaggerated as residues on soil that are exposed to sunlight yield a lower percent of MBC. This is evident based on review of the soil photolysis study, where at day 19.3, 23.6% of the total residue was thiophanate-methyl and only 20.8% of the residue was MBC. This was the highest level of MBC seen up to this final sampling point.**
46	**p. 44 ¶ 3**	**EPA used ornamentals - high rate for modeling of surface water. This is the drench rate and is not used on 100% of the crop. Elf Atochem will provide data on actual drench use at a later date.**
47	**p. 47, ¶ 2, line 3**	**The correct number of registrations is 36 active and 22 Special Local Need.**
48	**p. 47 - 4.3**	**This should say.....Major food/feed crops include: dry beans, sugar beets, wheat, potatoes, apples, green beans.**
49	**p. 47 last paragraph**	**The correct range of ai's is 1.65% - 90%.**
50	**p. 48 4.3.1**	**The title indicates that these mixing loading scenarios are for agricultural crops, however many of them represent strictly turf and ornamental usages: 8,9,10,15,16,18.**
51	**p. 48, ¶ 2**	**Granular products are not applied to turf using belly grinder applicators.**
52	**p. 49, ¶ 4**	**The Agency is assuming 35 years of applicator exposure while stating in the RED chapter on human exposure to TM is less than 6 years based on a survey of such workers.**

No.	Location	Error
53	**p. 49, ¶ 4**	**The default body weights are too low, especially as PHED is being used to model exposure rates. PHED was amassed using agricultural workers who were predominantly adult males. These individuals have body weights that exceed these default values. As PHED participants were heavier, they had a greater skin surface for available to exposure. Therefore, a correction factor should be applied when using PHED modeling for a population with a lower average body weight.**
54	**p. 51, ¶ 5**	**Industry data indicates that the average involvement for a PCO applicator is less than 3 years.**
55	**p. 53, ¶ 1**	**The REIs are exaggerated by the fact that the exposures the Agency is using to calculate them are not the only reasons for workers to reenter a treated area. For example, an orchard worker can walk through the aisles of an orchard long before the stated 15-105 day REI as long as he/she is not harvesting fruit. As TOPSIN M is applied throughout the growing season, the Agency should refine its REI assessments to reentry for more purposes than final harvest.**
56	**p. 53, ¶ 3**	**The EPA is using an unrealistic worst-case to model all greenhouse/ hothouse exposures. Per USDA figures, the cut-flower market constitutes less than 5% of the entire horticultural market in the USA. Perhaps the cut-flower scenario should be split off from the rest of the greenhouse/ hothouse scenarios.**
57	**p. 56**	**The application rates the Agency has proposed for the mixing/loading/applying of the WSB formulation for handgun application are too high. The top rate is 10.9 lb ai/ A and the typical application ranges form 2.7 to 5.5 lb ai/ A.**
58	**pp. 56-57**	**The application rates in scenarios 11 and 12 should agree but don't. See above comment for rates that should be used.**
59	**p. 57**	**Scenario 15: Belly grinders are used to apply granular formulations to beds and ground cover, not to turf.**
60	**pp. 59-60**	**Per agreement with the ARTF, the ARTF-developed transfer coefficients should be used for risk assessment. The values in the RED are too high when compared with empirically-derived data.**

No.	Location	Error
61	**p. 62, ¶ 1**	**The estimates of exposure for broadcast application of Scotts fertilizers containing TM were "based on treatment of 0.5 acre of lawn per day". Given the fact that this would require an unusually large lawn and, therefore, automated application equipment, the scenario is probably unrealistic. Otherwise, an average lawn is fertilized with TM-containing product only once per year and on one day per year only at the maximum.**
62	**p. 62, ¶ 1**	**The Professional Lawn Care Association of America (PLCAA) estimates that the average lawn is 5,000 square feet, which is 0.17 acre. The use of 0.5 and 0.3 acre lawns exaggerates the risk to homeowner applicators.**
63	**p. 62, ¶ 3**	**The Agency has modeled homeowner exposure on Scotts products but has assumed five applications per year, in contravention to Scott's recommendations. A fungicide-bearing fertilizer is applied only once per year and sometimes not at all.**
64	**p. 62, ¶ 4**	**Scenario 5 consists of residents' exposure to TM harvesting treated fruit in a home orchard despite the statement on p. 61, ¶ 1, that the current labels do not allow residents to treat home orchards. Moreover, in a domestic setting, residential fruit trees would be treated in the early season before fruit set (for scab prevention).**
65	**p. 63, ¶ 2**	**The Agency has assumed that TM is used to treat residential fruit trees in the same manner as it is used to treat commercial orchards. In the domestic setting, TM is applied only in the early season prior to fruit set, if at all. Therefore, there would be negligible exposure to TM or MBC at the time of harvest. These treatments prevent scab diseases on residential fruit trees which are usually ornamental in any case. The postulated home orchard where family members spend 20-40 minutes per day for 1-7 days per year is an unrealistic worst case.**
66	**p. 64, ¶ 4**	**Line 2: TOPSIN M is not applied in residential settings.**
67	**p. 72 ¶ 2**	**Statement that benomyl and TM are used on the same crops is in error; they are used on <u>some</u> of the same crops. Benomyl not labeled on potatoes, or t/o, and has many more crop uses.**

No.	Location	Error
68	**pg 72 end of ¶ 2**	**The annual usage for benomyl documented in Gianessi 1997 is 675,500 lbs ai vs the 1 million lbs ai listed here. TM is documented at 454,000 lbs ai for ag crops. Benomyl ai is 33% higher than TM, but lbs formulated is 1.35 million lbs benomyl (50%) vs. 650,000 lbs TM (70%) - benomyl is approx 2x acres treated based on lb formulated equivalent.**
69	**Page 72; ¶ 2; line 6**	**Monitoring data from USDA Pesticide Data Program (PDP) is available for MBC residues for certain food commodities. This data should be used for developing a more accurate risk assessment of MBC residue dietary exposure. It is also possible to approximate thiophanate-methyl residues at the consumer level by using the average ratio of TM to MBC within residue studies and applying the ratio factor to the PDP data. Because thiophanate-methyl residues dissipate more rapidly than MBC residues, such an assessment would still be very conservative.**
70	**Page 79; 5.4.1 Aggregate 1; line 3**	**Both aggregate assessments, TM and MBC (TM use) and TM and MBC (all uses) both yield a total thiophanate methyl and MBC dietary cancer risk of 2 E-6 (see Page 80; pp1; line 2). Based on page 82, Table 20, it would appear that 2 E-6 is an aggregate risk for TM and MBC (all uses).**
71	**Page 82; Table 20; lifetime cancer risk estimate**	**The lifetime cancer risk estimate for TM of 1.2E-7 is in error according to other EPA statements.**

ERROR COMMENTS
SECTION K
Revised Chronic Carcinogenic Dietary Risk Assessments for Thiophanate-methyl (TM) and its Metabolites Methyl 2-Benzimidazolyl Carbamate (MBC) and 2-Aminobenzamidazole (2-AB), dated May 10, 2000, DP Barcode D265906

Note: all comments relate to the March 16, 2000 memo from Lori L. Brunsman to Nancy McCarroll titled REVISED Thiophanate-methyl Quantitative Risk Assessment Based on Fischer 344 Rat and CD-1 Mouse Chronic Dietary Studies with 3/4's Interspecies Scaling Factor.

No.	Location	Error
1	**p. 1, ¶ 1**	**On page 1 of this memo, it is stated that : "The most potent unit risk, Q1* (mg/kg/day)-1, of those calculated for thiophanate- methyl is that for male mouse liver adenoma and/or carcinoma and/or hepatoblastoma combined tumor rates at 1.38 x 10-2 in human equivalents. The dose levels used from the 78-week dietary study were 0, 150, 640, 3000, and 7000 ppm of Thiophanate-methyl. The corresponding tumor rates were 4/47, 8/46, 8/47, 19/45, and 24/42, respectively."** **A rationale should be presented as to the reason(s) for combining tumor types. It is generally accepted that these tumor types may be combined in cases where there is evidence that there may be a temporally- and/or dose-related basis for suggesting a progression from adenoma to carcinoma. This theory, however, is clearly not supported by the incidence or time-to-tumor (carcinoma/blastoma) data in the present study.**
2	**p. 2, ¶ 2, line 3**	**On page 2, it is stated that "For the conversion to human equivalents, weights of *0.03 kg for the mouse … and the use of 78 weeks for the mouse life-span default … were used."*** **We believe that default values should not be used as a substitute for direct and factual data. Body weights of all animals were presented in the laboratory study report (MRID #42607701) and were reviewed by the Agency. The time-weighted average body weights of the CD-1 mice in this study significantly exceeded 0.03 kg. Animals that survived to termination were euthanized following a minimum of 79 weeks of dosing. The Q1* values should be re-calculated using case-specific data rather than generic default assumptions**

3	**general**	**The risk assessment memorandum does not disclose the values for average daily intake of test material that were used in calculating the Q1*. As noted in our previous comments, the values that were used in the Report of the Cancer Assessment Review Committee (8/24/99) contain significant errors.**